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TREATMENT OF BASAL CELL EPITHELIOMA BY INJECTION OF TISSUE EXTRACTS

A Preliminary Report

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A GREAT deal of research work has been done in an effort to find a way of treating cancer biologically by nondestructive methods, i. e., methods other than surgical intervention and irradiation. Early experimenters attempted to induce resistance in laboratory animals by inoculation with material from tumors. Ehrlich,[1] Lewin,[2] Képinow [3] and Koenigsfeld [4] reported successful results; however, Hertwig and Poll,[5] Borrel,[6] Gierke,[7] Fränkel and Fürer [8] and Wood [9] were unable

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† From the Skin and Cancer Unit, New York Post-Graduate Medical School and Hospital, Columbia University, as part of a collaborative research program with the Institutum Divi Thomae, Cincinnati.

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2. Lewin, G.: Die bösartigen Geschwülste, Leipzig, W. Klinkhardt, 1909.

3. Képinow, L.: De la résistance au cancer des souris préparées par injections répeteés de tissu cancéreux chauffé, Réunion Soc. belge biol., 1920, pp. 77-79; Physiol. Abstr. **5**:432-433, 1921; Chem. Abstr. **15**:3319, 1921.

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9. Wood, F. C., and Prigosen, R. E.: No Immunity Produced by Inoculating Irradiated Tumor Tissue, J. Cancer Research **9**:287-297, 1925.

to induce any resistance in their experimental animals. Since the different investigators did not use the same method of treatment, it is difficult to compare their results and to draw definite conclusions.

Almost coincidental with the work on the immunization of animals by tumor inoculations were investigations of the immunizing power of tissues other than neoplasms. Many tissues were used, but of particular interest in this paper are spleen and liver. Levin [10] was able to demonstrate the development of decided resistance to tumor growth by the injection of autolyzed liver of rats naturally resistant to the tumor. Levin [11] also reported positive results in experiments in which normal skin and spleen tissue of a mouse were inoculated subcutaneously into rats. Higuchi [12] reported some positive results in experiments using placenta, blood, embryonic skin, mammary gland and spleen to induce resistance against the carcinoma of the mouse. Itami [13] demonstrated the power of normal embryonic liver to induce resistance to transplantable tumors. Oser and Pribram [14] found that the injection of spleen pulp into sarcoma-implanted rats sometimes resulted in shrinkage of the tumors and at other times brought the tumor growth to a standstill. Büngeler,[15] using spleen implants on the Ehrlich adenocarcinoma and on a malignant chondroma of two weeks' growth, found little if any effect on the final development of the tumor. Fichera [16] transplanted bits of spleen and thymus from the fetus to cancerous patients, with little success. Later he prepared extracts from these organs which were used in treating 300 patients, 100 of whom had inoperable cancer. At the end of three years regres-

10. Levin, I.: Resistance to the Growth of Cancer Induced in Rats by Injection of Autolyzed Rat Tissue, Proc. Soc. Exper. Biol. & Med. **7**:64-67, 1909.

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14. Oser, E. G., and Pribram, E. E.: Ueber die Bedeutung der Milz in dem an malignem Tumor erkrankten Organismus und die Beeinflussung von Tumoren durch Milzbrei, Ztschr. f. exper. Path. u. Therap. **12**:295-302, 1913; Chem. Abstr. **8**:166, 1914.

15. Büngeler, W.: Die Bedeutung der Milz für das Wachstum und den Stoffwechsel maligner Tumoren, Frankfurt. Ztschr. f. Path. **43**:409-433, 1932.

16. Fichera, G.: Die biologische Krebsbehandlung und ihre Beziehung zu der Strahlentherapie der Geschwülste, Strahlentherapie **50**:302-311, 1934.

sions had occurred in 9 per cent of the patients and the tumors had become stationary in 8 per cent.

Even though there is substantial agreement on the power of some tissues to immunize or cause regression of a tumor, there has been decided disagreement as to whether or not the cells used for building resistance must be living. It seemed, however, that only living cells have this power, according to the experiments of Michaelis,[17] Ehrlich and Bashford (as cited by Levin [18]), Flexner and Jobling,[19] Woglom,[20] Haaland,[21] von Graff and Ranzi,[22] Pitzman [23] and Chambers and Scott.[24] In view of the limited or questionable success of experiments in which nonliving cells were used as the immunizing agent, it is not at all surprising that few reports of successful experiments are to be found in the literature on the use of cellular extracts as immunizing agents. Chambers and Scott [24] expressed the belief that the agent causing immunity to tumors in the case of the Jensen rat carcinoma was a soluble product of the dead tumor cells formed as a result of enzymatic action. Fardon,[25] using a strain of heterozygous market albino mice and the mammary adenocarcinoma 63, found that mice could be rendered resistant by injections of a cell-free extract of normal tissues. His results showed that the active immunizing fraction is water soluble, may be separated from the tissue pulp and need

17. Michaelis, L.: Versuche zur Erzielung einer Krebsimmunität bei Mäusen, Ztschr. f. Krebsforsch. **5**:191-197, 1907.

18. Levin, I.: Studies on Immunity in Cancers of the White Rat, J. Exper. Med. **12**:594-606, 1910.

19. Flexner, S., and Jobling, J. W.: Restraint and Promotion of Tumor Growth, Proc. Soc. Exper. Biol. & Med. **5**:16-18, 1907.

20. Woglom, W. H.: Resistance Produced in Mice Against Transplanted Cancer by Auto-Inoculation of the Spleen, J. Exper. Med. **12**:29-33, 1910.

21. Haaland, M.: The Contrast in the Reactions to the Implantation of Cancer After the Inoculation of Living and Mechanically Disintegrated Cells, Proc. Roy. Soc., London, s.B **82**:293, 1909; Lancet **1**:787-789, 1910.

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25. Fardon, J. C.: The Immunizing Property of Various Tissues and Tissue-Fractions to the Transplantable Mouse Adenocarcinoma 63, Bull. Basic Sc. Research **5**:5-12, 1933.

not be linked to the living cell. Domagk and Hackmann [26] also obtained satisfactory results with cell-free water extracts from tumor and from normal tissue. Using the Ehrlich mouse carcinoma, the Jensen rat sarcoma and the Brown-Pearce rabbit carcinoma, they obtained distinct resistance with the cell-free fraction against subsequent tumor implantation. In the case of established tumors, however, they found that large doses of the fraction stimulated the growth of the neoplasms.

As late as 1936 Murphy [27] stated that clearcut results had not been obtained in attempts to influence susceptibility with serum and with tissue and organ extracts, but definite resistance to transplantable tumors had been obtained only in the early investigations in which living homologous normal cells were used. Lewisohn [28] tested the effect of a water-soluble beef spleen extract on mouse sarcoma 180. Of the 281 treated sarcomas, 60 per cent were absorbed and considered as healed with no recurrence during a period of five months, while 8 per cent of the 290 controls were found to have regressed spontaneously. He reported that low concentrations of the extract had great stimulatory effects on the tumors. Fardon [25] demonstrated that the immunizing principle from spleen extracts was not a protein fraction. In fact, in his experiments he demonstrated that increased susceptibility resulted from the injection of the protein fraction. Bauer and others [29] carried out an investigation on 879 mice with transplantable Ehrlich carcinoma. They concluded that the alcoholic extract of the spleen tissue had an inhibiting action on the development of tumors and that purification of the extract with benzene doubled the activity of the extract. Lewisohn and others [30] precipitated the protein fraction from their extract and introduced their fraction intravenously rather than subcutaneously. This method of administration was successful, but the effects followed a different course from those obtained by subcutaneous injections.

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26. Domagk, G., and Hackmann, C.: Ein Beitrag zu den bei Transplantattumoren beobachteten Immunitäts- resp. Resistenzerscheinungen, Ztschr. f. Krebsforsch. **42**:192-208, 1935; Am. J. Cancer **25**:825, 1935.

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28. Lewisohn, R.: Effect of Subcutaneous Injections of Concentrated Spleen Extract on Mouse Sarcoma 180, Surg., Gynec. & Obst. **66**:563-576, 1938.

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30. Lewisohn, R.; Leuchtenberger, R., and Laszlo, D.: Spleen Extract in the Treatment of Transplanted and Spontaneous Malignant Tumors in Mice, Surg., Gynec. & Obst. **71**:274-285, 1940.

In connection with the work on immunity and regression of tumors, the metabolism of cancerous tissue is of interest. Warburg,[31] in his epoch-making researches, reported that the respiration of carcinoma tissue was less than that of kidney and liver. In spite of the breakdown of some of Warburg's original claims, Burk[32] has upheld the contention that malignant tissues differ from normal ones in their metabolism. He pointed out that the sum of many metabolic characteristics must be taken into consideration for full differentiation between normal and malignant tissues. Amersbach, Walter and Cook[33] found alterations in the respiration of precancerous lesions and epitheliomas from that of the normal epithelium of the same general area. Davis[34] and Büngeler[35] found that the respiration of normal tissues of a strain of mice which is resistant to a transplantable tumor is considerably higher than the average respiration of the normal tissues of a susceptible strain. Büngeler demonstrated the power of a fairly crude spleen extract to stiumlate the respiration and depress the glycolysis of tumors. Sperti[36] described the respiration-stimulating power of a beef spleen extract on a mouse sarcoma. Fardon, Brotzge and Loeffler[37] observed that "an injection of placental suspension (immunizing agent) into mice definitely stimulates the oxygen consumption of the skin." Schroeder and Cook[38] found that extracts

31. Warburg, O.: The Metabolism of Carcinoma Cells, J. Cancer Research **9**:148-164, 1925.

32. Burk, D., in Ward, H. B.: Some Fundamental Aspects of the Cancer Problem, New York, The Science Press, 1937, p. 121; On the Specificity of Glycolysis in Malignant Tumors as Compared with Homologous Adult or Growing Liver Tissues, in A Symposium on Respiratory Enzymes, Madison, University of Wisconsin Press, 1942, pp. 235-245. Burk, D.; Sprince, H.; Spangler, J. M.; Kabat, E. A.; Furth, J., and Claude, A.: The Metabolism of Chicken Tumors, J. Nat. Cancer Inst. **2**:201-240, 1941.

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36. Sperti, G. S.: Radiations, Cellular Metabolism and Cancer Resistance, Stud. Inst. Divi Thomae **3**:17-38, 1941.

37. Fardon, J. C.; Brotzge, G. C., and Loeffler, Sister M. K.: The Relation of Induced Tumor Resistance to Increased Tissue Respiration, Stud. Inst. Divi Thomae **3**:61-68, 1941.

38. Schroeder, Sister M. P., and Cook, E. S.: The Effects of Tissue Extracts on the Respiration and Glycolysis of Some Normal and Tumor Tissues, Stud. Inst. Divi Thomae **2**:247-258, 1939.

from yeast and normal tissues increase respiration and depress both the aerobic and anaerobic glycolysis of normal liver and tumor tissues.

There seems to be evidence to indicate that agents which have the power to build resistance to tumor growth may have the power to affect the metabolism of malignant tissues. However, it has not been demonstrated that all substances which have the power to stimulate respiration likewise have the power to induce the resistant state.

The interrelation between respiration and glycolysis, and immunity to tumors, is discussed at some length by Sperti [36] in a review on cellular metabolism and resistance to cancer.

Since it had been shown that spleen and liver extracts gave good results in the experiments on animals and the extracts seemed to have a beneficial result on the metabolism of cancerous tissue, it was decided to test their effect in the treatment of human epitheliomas. Tumors of low malignancy, which were localized and easily accessible, were used to make certain that any effectiveness of the fraction could be readily observed. Basal cell epitheliomas seemed to offer the best type of neoplasm for the investigations.

THE PREPARATION OF SPLEEN AND LIVER EXTRACTS

Normal human spleens and livers were collected at autopsy. In all cases care was taken not to use tissues from cadavers which had been standing more than twenty-four hours. Only those of persons who had died suddenly, as a result of accident or heart disease, were used.

The liver and spleen extracts were prepared separately. The tissues were weighed, trimmed of all fat and extraneous connective tissue and ground thoroughly and added to a volume of distilled water corresponding to the weight of the tissue, i. e., 100 cc. of water per hundred gram of spleen. The suspension was frozen and thawed three times, allowing one day for each freezing and thawing procedure. The proteins were then precipitated by adding increasing concentrations of 95 per cent alcohol to the mixture. First, alcohol was added to a final concentration of 50 per cent, and the mixture was allowed to stand for two hours. Finally, the concentration was raised to 80 per cent, the mixture allowed to stand for one day and filtered free of tissue and precipitated protein. The extract was concentrated approximately to the volume of distilled water added originally. This water solution was then extracted with three separate portions of ether of a total volume equal to that of the water solution. The ether solution was discarded, and the water solution was evaporated almost to dryness. The residue was made up to the desired concentration with distilled water.

In the earlier work a concentration of 1 cc., equivalent to 1 Gm. of tissue, was used; that is, the volume of the final solution was the same in cubic centimeters as the weight in grams of the tissue extracted. In the later work a concentration of 1 cc., equivalent to 9 Gm., was used; that is, a volume equal to one ninth of the weight of the tissue in grams. The p_H of the extract was adjusted to 6.5 to 7 with potassium hydroxide, and the extract was boiled for thirty minutes. After standing in the refrigerator overnight, the solution was filtered. The extract was then put into serum bottles and boiled for thirty minutes on each of three successive days. Each sample of extract prepared was

tested for toxicity by injecting into a guinea pig the same amount to be used subsequently on the patients. In no case were any ill effects shown by the animals or the patients.

CLINICAL PROCEDURE

At the Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, patients were selected with small basal cell epitheliomas varying in size from that of a pea to 3 or 4 cm. in the longest dimension. All types of basal cell epitheliomas were taken indiscriminatelyl as they appeared in the clinic service. Before any treatment was given, a colored photograph was taken of the lesion and a biopsy was also performed for pathologic diagnosis of the lesion. The patient was then given a series of weekly injections of either spleen or liver extract and observed closely. The patient occasionally missed an injection, or occasionally it was deemed advisable to allow a longer time to elapse between the injections, as for example, when a crust was present.

Injections were made intradermally, for it has been shown repeatedly by Besredka and Gross [39] that the intradermal route was successful; they produced immunity to tumors in animals by the intradermal injection of tumor suspension. Cheever and Janeway [40] also used the intradermal method in successfully inducing resistance against the Brown-Pearce carcinoma. Generally 1 cc. of extract was injected, although when the location was such or the lesion had regressed until it was very small only 0.25 cc. or 0.5 cc. was used. Occasionally if the lesion was large 1.5 cc. or 2 cc. of extract was necessary to infiltrate it well. At each treatment the lesion was infiltrated until it and the surrounding tissue for about ¼ inch (0.6 cm.) became blanched and hard.

In some cases, especially with the liver extract, the patients found the injections painful and a small amount (0.25 to 1 cc.) of 2 per cent solution of epinephrine-free procaine hydrochloride was given a few minutes preceding the injection. Some patients received no procaine, and others did not receive it at all injections. Procaine did not seem to influence the course of the regression of the lesion.

It was thought that the regression of the epitheliomas to the extract might be nonspecific and was due simply to a sclerosing action of the material. It was therefore decided to treat several patients with a dextrose solution of a concentration equal to that of the spleen extract, which was 275 mg. per cubic centimeter. Dextrose was employed because it is successfully used in the clinic for sclerosing varicose veins. Four patients were given the control dextrose solution at weekly intervals and observed carefully. Each received from five to seven injections, which number had been more than sufficient to elicit a response with the extracts. When all lesions failed to respond, photographs were taken and the patients were given liver or spleen extract.

A further check was made on the specificity of the extracts by testing them on normal skin. Intradermal injections of the dextrose solution and the liver

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39. Besredka, A., and Gross, L.: Du role de la peau dans la sarcomatose de la souris, Ann. Inst. Pasteur **55**:402-416, 1935; De l'immunisation contre le sarcome de la souris par la voie intracutanée, ibid. **55**:491-500, 1935. Gross, L.: Experimental Immunization Against Implantation of Cancer, Quart. Bull. Polish Inst. Arts & Sc. America **1**:418-430, 1943.

40. Cheever, F. S., and Janeway, C. A.: Immunity Induced Against the Brown-Pearce Carcinoma, Cancer Research **1**:23-27, 1941.

Case Histories of Patients Treated with Tissue Extracts

Case	Sex	Age	Location and Description of Lesion	Pathologic Report	Treatment	Duration of Treatment	Result
Preliminary R. W.	M	41	Pea-sized lesion with rolled pearly borders and central ulceration on right side of nose	Basal cell epithelioma	Spleen; 7 injections, 1 cc. = 1 Gm.; 8 injections, 1 cc. = 3 Gm., 1 cc. each injection	3/25/42 to 5/6/42	Definite regression but patient failed to continue treatment
Preliminary I. R.	F	55	Pea-sized lesion with typical rolled pearly borders on center of forehead	Basal cell epithelioma	Spleen; 7 injections, 1 cc. = 6 Gm., 1 cc. each injection	7/27/42 to 10/2/42	Definite regression but patient failed to continue treatment
1 E. Y.	F	61	Pea-sized raised lesion on preauricular region	Basal cell epithelioma	Spleen; 8 injections, 1 cc. = 6 Gm.; 16 injections, 1 cc. = 9 Gm., 1 cc. each injection	1/20/43 to 7/28/43	Complete regression
2 J. M.	M	60	Dime-sized raised ulcerated lesion with pearly borders on left temple	Basal cell epithelioma	Spleen; 10 injection, 1 cc. = 6 Gm.; 3 injections, 1 cc. = 8 Gm.; 2 injections, 1 cc. = 9 Gm., 1 cc. each injection	1/25/43 to 5/3/43	Complete regression
3 I. W.	M	81	Dime-sized red lesion with slightly raised borders on back of right hand	Senile keratosis	Spleen; 10 injections, 1 cc. = 9 Gm., 1 cc. each injection	6/7/43 to 10/27/43	Complete regression
4 J. M.	F	75	Large pea-sized lesion with rolled waxy borders on forehead	Basal cell epithelioma	Spleen; 2 injections, 1 cc. = 8 Gm.; 6 injections, 1 cc. = 9 Gm., 1 cc. each injection	5/24/43 to 8/6/43	Complete regression
5 M. K.	F	71	Large raised pearly pea-sized lesion on right side of nose	Basal cell epithelioma	Spleen; 6 injections, 1 cc. = 9 Gm., 1 cc. each injection	6/30/43 to 8/4/43	Complete regression
6 T. G.	M	71	Pea-sized raised pearly lesion just under left eyelid	Basal cell epithelioma	Spleen; 20 injections, 1 cc. = 9 Gm.; 2 injections, 1 cc. = 15 Gm., 1 cc. each injection	7/21/43 to 5/31/44	Failed to regress
7 M. P.	M	33	Pea-sized elevated lesion with pearly wall and crust formation on right nasolabial fold .	Basal cell epithelioma	Dextrose; 7 injections, 275 mg./cc. Spleen; 7 injections, 1 cc. = 9 Gm.	8/16/43 to 10/20/43 10/27/43 to 2/9/44	No apparent response to dextrose Complete regression
8 B. A.	M	83	Large lesion, 3 by 1.5 cm., with rolled pearly edges and central ulceration	Basal cell epithelioma	Dextrose; 5 injections, 275 mg/cc. Spleen; 17 injections, 1 cc. = 9 Gm., 1 cc. each injection; 8 injections, 1 cc. = 15 Gm., 0.5 cc. each injection	9/15/43 to 10/13/43 10/27/43 to 9/20/44	No apparent response to dextrose Still under treatment; approximately 80% regression
9 E. P.	F	51	Finger-nail-sized area, studded with waxy hard transparent nodules on left cheek	Basal cell epithelioma	Dextrose; 5 injections, 275 mg./cc. Liver; 18 injections, 1 cc. = 9 Gm.; 6 injections, 1 cc. = 15 Gm. 1 cc. each injection	9/15/43 to 10/20/43 11/3/43 to 10/30/44	No apparent response to dextrose Still under treatment; approximately 75% regression

10 A. R.	F	65	Large pea-sized crusted lesion with rolled border on left preauricular region	Spinobasal cell epithelioma	Liver; 10 injections, 1 cc. = 9 Gm.; Liver; 1 injection, 1 cc. = 15 Gm. 0.5 cc. each injection	10/6/43 to 6/5/44	Complete regression
11 D. R.	M	67	Pea-sized infiltrated ulcerated lesion on right ear	Basal cell epithelioma	Dextrose; 6 injections, 275 mg./cc.	10/4/43 to 11/8/43	No apparent response to dextrose
					Spleen; 3 injections, 1 cc. = 9 Gm., 1 cc. each injection	12/13/43 to 1/5/44	Complete regression
12 M. M.	M	64	Dime-sized ulcerated lesion with pearly borders on right cheek	Basal cell epithelioma	Liver; 15 injections, 1 cc. = 9 Gm., 1 cc. each injection; 3 injections, 1 cc. = 15 Gm.; 0.5 cc. each injection	10/4/43 to 7/12/44	Still under treatment; approximately 90% regression
13 C. S.	M	57	Dime-sized lesion with slightly rolled borders on forehead	Basal cell epithelioma	Liver; 4 injections, 1 cc. = 9 Gm., 1 cc. each injection; 8 injections, 0.25 cc.	10/13/43 to 7/26/44	Complete regression
14 G. S.	M	79	Dime-sized raised crusted lesion on right breast	Basal cell epithelioma	Spleen; 19 injections, 1 cc. = 9 Gm., 1 cc. each injection	10/25/43 to 5/8/44	Approximately 50% regression; patient failed to return for treatment
15 M. B.	F	50	Dime-sized ulcerated lesion with pearly borders on left cheek near eye	Basal cell epithelioma	Liver; 21 injections, 1 cc. = 9 Gm., 1 cc. each injection; 3 injections, 1 cc. = 15 Gm., 0.5 cc. each injection	10/27/43 to 7/5/44	Complete regression
16 L. S.	M	53	Large, pea-sized, infiltrated lesion with pearly borders and central ulceration on left temple	Basal cell epithelioma	Liver; 8 injections, 1 cc. = 9 Gm., 1 cc. each injection	11/1/43 to 12/20/43	Complete regression
17 W. M.	M	68	Dime-sized pigmented lesion on left preauricular region	Seborrheic verruca with intraepidermic basal cell epithelioma	Spleen; 6 injections, 1 cc. = 9 Gm. 1 cc. each injection	11/15/43 to 12/20/43	Complete regression
18 R. W.	M	75	Half-dollar-sized brown smooth pearly lesion on back of neck	Basal cell epithelioma	Spleen; 4 injections, 1 cc. each injection; 3 injections, 1.5 cc. each injection; 7 injections, 2 cc. each injection, 1 cc. = 9 Gm.; 3 injections, 1.5 cc. each injection; 5 injections, 1 cc. each injection, 1 cc. = 12 Gm.	12/15/43 to 11/8/44	Still under treatment; 80% regression
19 F. G.	F	49	Pea-sized, slightly elevated, pigmented lesion with central depression on lateral border of left side of nose	Basal cell epithelioma	Spleen; 15 injections, 1 cc. = 9 Gm., 0.5 cc. each injection; 12 injections, 1 cc. = 12 Gm., 0.25 cc. each injection	12/20/43 to 10/4/44	Still under treatment; approximately 30% regression
20 M. D.	F	70	Dime-sized eroded lesion with pearly border on right preauricular region	Basal cell epithelioma	Spleen, 6 injections, 1 cc. = 9 Gm., 1 cc. each injection	1/3/43 to 4/24/44	Complete regression
21 M. L.	F	35	Pea-sized raised pearly lesion on center of forehead	Basal cell epithelioma	Liver; 8 injections, 1 cc. = 9 Gm., 0.5 cc. each injection	2/23/44 to 4/12/44	Complete regression

and spleen extracts were made into the normal skin on the upper part of the arms and the thighs, 2 or 3 patients being used for each solution. In each patient the inflammation and swelling characteristic of the intradermal injection of a nonisotonic solution were noted. With the liver extract a small dark discolored area was produced, which became bullous and later produced a thin crust. This may have been an effect of the concentration. However, since the spleen extract never produced such an area and also was active in causing the regression of the basal cell epitheliomas, it seems likely that the active factor is probably nontoxic to normal skin.

The case histories are given in the table, and photographic histories of several of the cases are shown.

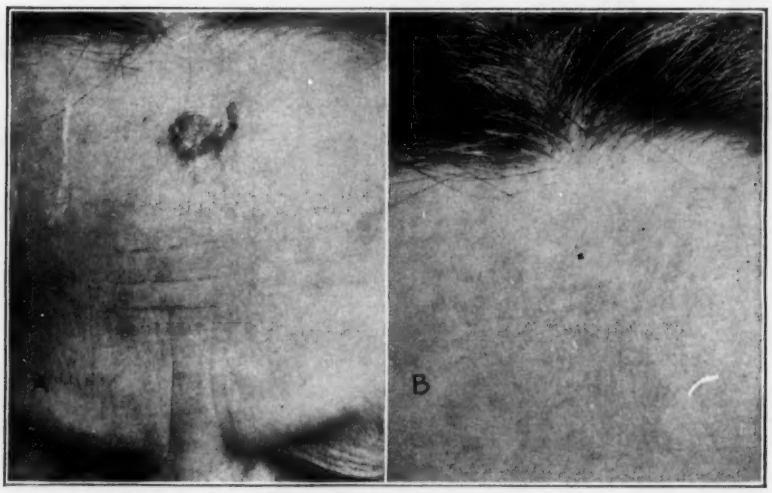

Fig. 1 (case 4).—*A*, before treatment; *B*, after treatment with eight injections of spleen extract.

COMMENT

In these experiments, 21 patients with basal cell epitheliomas were treated with extracts of liver or spleen. One patient (case 6) receiving the spleen extract failed to respond to the treatment. Of the other 20 patients, 14 continued the treatment to complete regression of the lesion as observed clinically and as shown by final biopsy of the lesion. The other 6 patients are still under treatment, but all have shown definite regression of the lesion. In some of the finished cases the cosmetic result is indeed excellent, for no scar is visible; in others, there is a scar similar to that resulting from excision, probably dependent on the amount of ulceration originally present. Four of the patients were first used as controls and given injections of a dextrose solution. All failed to respond to the injections of dextrose and were subsequently transferred to spleen or liver extract, where-

upon the lesions began to regress. In 2 cases (cases 7 and 11) the regression was rapid and required seven and three injections respectively. Lesions in the other 2 cases have been much slower to regress and have required a relatively large number of injections.

Of the 21 patients, 7 received liver extract and 14 spleen extract. It is difficult to say whether or not the spleen extract is more effective than the liver extract, for the size, type and location of the lesion and the general physical status of the patient varied greatly. In general, it appeared that the spleen extract produced a faster reaction than the liver extract.

Fig. 2 (case 15).—*A*, before treatment; *B*, after treatment with twenty-four injections of liver extract.

The number of injections required to cause complete regression varied a great deal according to the lesion. One patient required only three injections, several only six injections and some as many as twenty. It was noticed that in areas easily infiltrated with 1 cc. of extract the lesion responded much faster than in those around the eyes and on the nose. In the latter areas generally a smaller quantity of extract was used per injection, but the response was much slower even when the total quantity of extract used was the same as that employed in treating lesions which received a larger dosage per injection. It seems that a definite minimum dose per injection is required. Also, patients who were more regular in their treatments generally responded faster.

It is likely that the composition of the extracts varied, for several different preparations were used during the course of treatment, and,

although the same method of preparation was rigidly followed and only healthy tissue was used, there were probably individual variations in the tissue employed for the preparation of successive extracts.. In the early part of the work the spleens and livers were often from

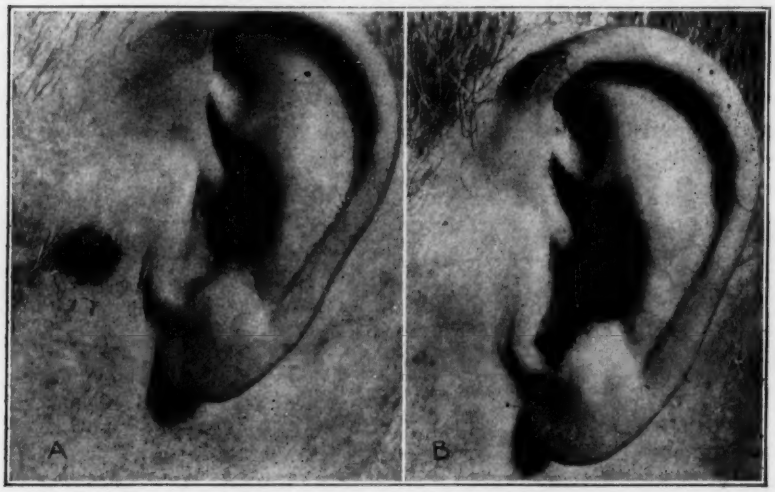

Fig. 3 (case 17).—*A*, before treatment; *B*, after treatment with six injections of spleen extract.

Fig. 4 (case 20).—*A*, before treatment; *B*, after treatment with six injections of spleen extract.

young cadavers, but recently the tissue has been almost wholly from middle-aged and older persons. The effect of the variations in the source of tissue used is not known and should be investigated.

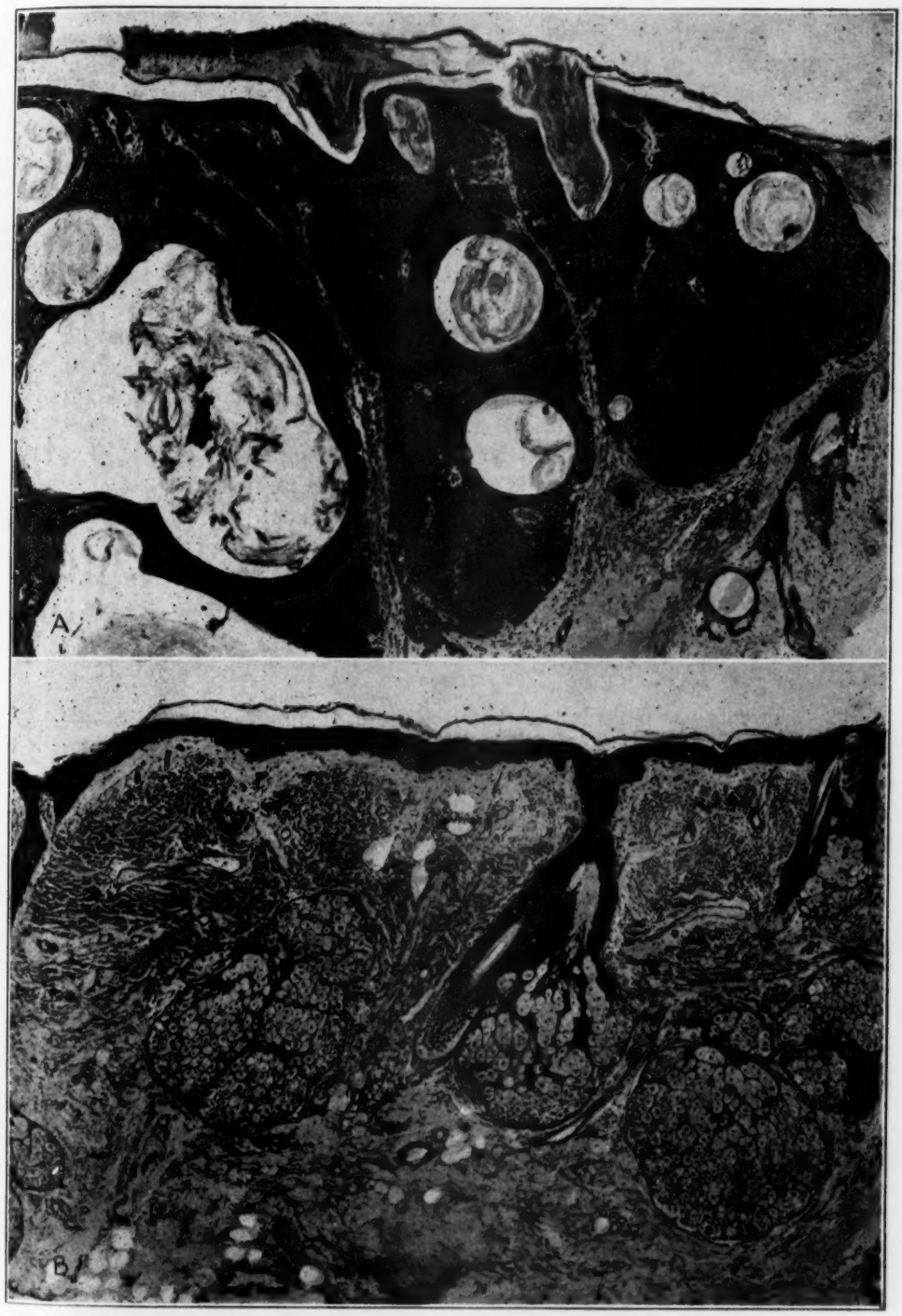

Fig. 5 (case 17).—*A*, pathologic section before treatment; *B*, pathologic section after treatment with six injections of spleen extract.

The lesion usually responded noticeably after the third or fourth injection, when there was a definite shrinking. In several cases the lesion appeared to regress by 50 per cent during one week between injections. A crust was generally present at some time during the regression of a lesion; in some cases the crust was thin and was replaced a number of times until the healthy tissue was finally revealed. In other cases the crust produced was dense and adhered firmly to the lesion for a number of weeks.

The extract seemed to have no effect on normal tissue, for only the lesion was affected, although the surrounding normal tissue was infiltrated at each injection. In the case that failed there was no noticeable change in lesion or surrounding tissue. Injections of spleen and liver extract into normal skin resulted in no toxic effect with the spleen extract but a slight reaction with the liver extract. Since both extracts were active in producing regressions of the epitheliomas, it seems that the active factor is probably not toxic to normal tissues.

In none of the cases observed since completion of the treatment has there been any signs of recurrence in the period of one to two years. However, it is too early to make any definite statement regarding recurrences, and the patients will be examined regularly over a period of at least five years.

SUMMARY

Twenty-one patients with basal cell epithelioma were treated by the injection of spleen or liver extract. The lesion of 1 treated with spleen extract failed to regress. Fourteen have had complete regression and disappearance of the lesion. The remaining 6 are still under treatment, but all have shown regression.

Dr. John B. Lauricella made it possible to obtain the tissue for preparation of the extract, and Dr. Wilbur Sachs made the pathologic diagnosis of the lesions.

SCLERODERMA OF THE FACE INVOLVING THE GINGIVA

Report of a Case

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WHILE cases of scleroderma are frequently encountered in clinic and private dermatologic practice, there seems to be little mention of oral involvement in the literature or in society transactions. Barber [1] in January 1944 described a man aged 43 with a sclerodermatous lesion confined to the mucous surface of the lower lip, extending from the vermilion border to the alveolar sulcus. He also cited a report by W. Anderson, in 1898, of a case of scleroderma involving the skin and mucous membranes supplied by all three divisions of the fifth cranial nerve. Looby and Burket [2] in 1942 reported a case of scleroderma of the face with involvement of the alveolar process. Their patient was an 8 year old girl on whose face there suddenly developed an indurated area roughly outlining the terminal distribution of the sensory divisions of the fifth nerve. She showed "deep scarring of the gingival tissue and depression of the alveolar process which, in the region of the left maxillary incisor, extended from the ridge toward the muco-buccal fold." Their paper gives an account of the historical development of the disease as well as an excellent review of the histologic features and etiologic possibilities. In 1933 a case of involvement of the skin and the buccal mucosa in a 57 year old woman was presented by Gougerot and Eliascheff [3] before a French dermatologic society. O'Leary and Nomland [4] in an extensive clinical study of 103 cases of scleroderma (55 of which were of the circumscribed type) did not mention mucosal involvement in any of them. This strengthens our conviction that circumscribed scleroderma involving the oral cavity is of sufficient rarity to warrant reporting.

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1. Barber, H. W.: Circumscribed Scleroderma of Buccal Mucous Membrane, Proc. Roy. Soc. Med. **37**:73 (Jan.) 1944.

2. Looby, J. P., and Burket, L. W.: Scleroderma of Face with Involvement of Alveolar Process, Am. J. Orthodontics **28**:493-498 (Sept.) 1942.

3. Gougerot and Eliascheff, O.: Scleroderma of Buccal Mucosa and Skin, Bull. Soc. franç. de dermat. et syph. **40**:111-112 (Jan.) 1933.

4. O'Leary, P. A., and Nomland, R.: Clinical Study of 103 Cases, Am. J. M. Sc. **180**:95-112 (July) 1930.

REPORT OF A CASE

E. D., a 20 year old white woman, was seen in March 1945; she had first noticed whitish depigmentation of the tip of her nose, of the cleft of her upper lip and of a vertical midline area on her forehead in December 1944. The general examination and past history were noncontributory. The area became progressively whiter, with a faint violaceous halo at the border. On the buccal surface of her upper lip was a vertical area lighter in color than the surrounding mucosa; this extended on the gingival margin to the right upper incisor, at which point the adjacent gingiva appeared necrotic.

Biopsy of a specimen from the mucosa under the upper lip showed a broad area in the submucosa of nearly acellular and very dense collagen in which the outlines of the fibrils were indistinct. A pathologic diagnosis of scleroderma of the labial mucosa was made (Dr. Warren C. Hunter).

Scleroderma involving the gingiva.

COMMENT

In the differential diagnosis of this case, vitiligo was strongly considered (at the first examination only the alabaster-like color of the skin was noted—induration was never a conspicuous feature). This diagnosis did not explain the lesion of the gingiva, a type of lesion which neither of us had observed before. Two dentists to whom the patient was shown expressed the opinion that the gum showed an "advanced degree of pyorrhea," although they could not explain its localization about a single tooth. Histologic examination of the gingival tissue established the diagnosis of scleroderma beyond reasonable doubt.

SUMMARY

A case of circumscribed scleroderma of the face involving the gingiva is described. Judging from available reports, such cases are comparatively uncommon.

Dr. L. S. Selling permitted us to study and report this case.

Medical-Dental Building.
Medical Arts Building.

USES AND ABUSES OF PENICILLIN IN DERMATOLOGY

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THE RECENT widespread employment of penicillin in the treatment of infectious dermatoses makes desirable a summary of the indications for and the contraindications to its use, as well as an analysis of the results to be expected from various methods of administration.

As reported in a previous communication,[1] penicillin in a water-soluble ointment base was used in the treatment of 40 patients with treatment-resistant cutaneous infections. None of the patients had previously received penicillin therapy. Cure was obtained in 66.6 per cent of patients with uncomplicated pyoderma, with the individual manifestations responding as follows: impetigo 85.7 per cent, pustular folliculitis 66.6 per cent, sycosis 60 per cent and infectious eczematoid dermatitis 55.5 per cent. Tests for sensitivity to penicillin were made on most of the patients. The trench plate method was used. In this procedure a trench was made across a blood agar plate by removing a strip 1 cm. in width. This trench was filled with agar containing 2 units of penicillin per cubic centimeter. The organism to be tested and the Florey strain of Staphylococcus aureus were then streaked across the trench. Sensitivity of the organisms to penicillin was shown by inhibition of growth comparable to that seen with the control.

It was found that when the causative organisms remained consistently sensitive to penicillin clinical involution of the lesions was constant, regardless of the type of cutaneous infection present. Resistance to penicillin as determined by this method, was found initially in 22.5 per cent of the cases. Follow-up tests of sensitivity to penicillin tests on patients with only temporary improvement or with relapsing lesions disclosed that an additional 15 per cent of infections had become resistant to penicillin. This phenomenon was thought to be due to the use of an inadequate concentration of penicillin, the strength of the ointment being 200 units of the drug per gram of ointment base.

This paper was prepared while the authors were in service with the Army of the United States.

1. Cormia, F. E., and Maschmeyer, R. H.: Therapy of Treatment-Resistant Pyoderma with Penicillin, M. Bull. Europ. Theat. Op., 1944, no. 23, p. 1.

The amount of penicillin was accordingly increased to 500 units per gram of base, and further resistance to penicillin did not develop.

Many questions, however, remained unanswered. Could optimum results be obtained from topical applications alone or from the simultaneous use of intramuscular injections? The results of the combined or alternate use of penicillin and the sulfonamide compounds were another matter for conjecture. Furthermore, would increasing local concentrations of penicillin be of value in treatment of infections in which the organisms manifested an increased resistance to penicillin? Lastly, the question of the use of penicillin empirically in treatment of severe infections, i. e. without a preliminary determination of sensitivity to penicillin, was opened to careful scrutiny.

MATERIALS AND METHODS

A group of 75 patients with treatment-resistant pyoderma was selected for study. The types of pyoderma investigated included impetigo, ecthyma, pustular folliculitis, sycosis, infectious eczematoid dermatitis, furunculosis, infected sebaceous cysts and secondarily infected acne vulgaris. The etiologic agent, with but few exceptions, was a pigmented coagulase-positive hemolytic Staph. aureus. Hemolytic Staphylococcus albus was found in 2 instances and a hemolytic streptococcus in 5. However, the hemolytic streptococcus was the sole pathogen in only 1 patient. The group of 75 patients differed from the first in two particulars. In the first place, the infections were much more chronic when first seen, and the patients had been treated unsuccessfully in from one to four general hospitals. Secondly, penicillin, in various doses and methods of administration, had been given to approximately 75 per cent of the patients. The sensitivity of the organisms to penicillin was determined by the filter paper technic, which will be discussed briefly in a later section.

Cultural studies revealed that the causative organisms in 75 per cent of the infections were insensitive to penicillin in a strength of 2 units per cubic centimeter. It should be emphasized at this point that sensitivity to penicillin in a strength of 2 units per cubic centimeter does not represent the amount of penicillin per cubic centimeter of agar, as was the case in the agar trench method. It represents, instead, the concentration of the penicillin solution which is used to moisten the disks of filter paper. Since an individual filter paper as used in this survey absorbed approximately 0.003 cc. of solution, it is apparent that the disk moistened with this solution contained only a small fraction of a unit. However, as will be shown later, 500 units of penicillin per gram of ointment base proved effective only when the causative organisms were sensitive to penicillin in a concentration of not more than 2 units per cubic centimeter by the filter paper method. It follows, then, that the data on sensitivity for the earlier series are misleading and that the actual sensitivity of the organisms to penicillin would probably take place with a strength much less than 2 units of penicillin per cubic centimeter of agar. On the basis of a recent experiment with the pour plate method of penicillin assay and use of the Florey strain of Staph. aureus, the true readings in most instances were probably in the region of $\frac{1}{10}$ unit of penicillin per cubic centimeter of agar.

The question was then raised as to whether or not cure could be obtained when penicillin sensitivity tests revealed that the test organisms were sensitive to penicillin only in concentrations greater than 2 units per cubic centimeter by the

filter paper method. On testing with serial strengths of penicillin, it was found that the sensitivity of the organisms in different patients varied from sensitivity to 1 unit per cubic centimeter to insensitivity to 2,000 units per cubic centimeter, while the control Florey strain of Staph. aureus remained uniformly sensitive at 1 to 2 units per cubic centimeter. As the study progressed, it became apparent that only in the patients with sensitivity to penicillin in concentrations of less strength (from 1 to possibly 20 units per cubic centimeter) could cures be obtained with the concentrations of penicillin used ordinarily in treatment. Of the group of 75 patients, the causative organisms were sensitive to penicillin in this range in 64 per cent. It seemed important, therefore, to determine the response of this comparatively large group to varying doses of penicillin administered both locally and systemically and given with or without supplemental therapy with sulfonamide compounds.

RESULTS OF TREATMENT

Treatment with Penicillin Ointment in Strength of 500 Units per Gram.—Treatment for the first 20 patients consisted of the use of an ointment containing 500 units of sodium penicillin per gram of ointment base. The penicillin was dissolved in a small amount of distilled water and incorporated in a water-soluble ointment base, composed of 15 per cent Lanette wax and 15 per cent petrolatum in water. The ointment base was not sterilized, since in the previous series an aseptic technic did not result in a greater percentage of cures. The 20 patients were unselected and included those with all types of pyoderma. Moreover, the causative organisms were sensitive to penicillin in concentrations ranging from 1 to 2,000 units per cubic centimeter.

When the causative organisms were sensitive to penicillin in a strength of 1 to 2 units per cubic centimeter, cure was invariable, regardless of the nature of the presenting cutaneous infection. If the organisms were sensitive only to concentrations of penicillin greater than 2 units per cubic centimeter cure did not occur. For a patient with infectious eczematoid dermatitis, the organisms of which were sensitive to penicillin in a strength of 8 units per cubic centimeter, clinical arrest was obtained on two occasions, but relapse occurred promptly after discontinuance of therapy. In a second patient, with sycosis vulgaris and with organisms sensitive to penicillin in a strength of 8 units per cubic centimeter, there was a temporary improvement of 30 per cent, but this was followed by clinical progression. A third, with infectious eczematoid dermatitis with organisms sensitive to penicillin in a strength of 50 units per cubic centimeter, showed only transient improvement. In the remaining patients, in whom the causative organisms were sensitive to penicillin within a range of 10 to 2,000 units per cubic centimeter, no improvement was seen.

Treatment with Penicillin Ointment in Concentrations Greater than 500 Units per Gram.—Varying concentrations of penicillin were used on a group of 15 patients in whom the organisms were sensitive to penicillin in concentrations ranging from 4 to 2,000 units per cubic

centimeter. Penicillin ointment containing 1,660 units per gram was used for 3 patients, 1 with impetigo and 2 with infectious eczematoid dermatitis, with the organisms sensitive to penicillin in strengths of 10, 50 and 100 units per cubic centimeter, respectively. None of these patients was improved after two weeks of therapy. One patient with impetigo, with the organisms sensitive to penicillin in a concentration of 2,000 units per cubic centimeter was not improved by penicillin ointment containing 3,330 units per gram. One patient with chronic sycosis, the organisms of which were sensitive to penicillin in a dilution of 100 units per cubic centimeter, was unimproved after use of penicillin ointment containing 3,330 units per gram.

The next 2 patients were of special interest. In the first a severe infectious eczematoid dermatitis of the face had developed some two months previously with a residual treatment-resistant sycosis of the bearded region. Culture yielded a coagulase-positive hemolytic Staph. aureus, sensitive to 50 units of penicillin per cubic centimeter. Treatment was instituted with penicillin ointment, 10,000 units per gram, three times daily, but no improvement ensued after six days, at which time a repeated culture showed that the organisms had become resistant to penicillin in a strength of 500 units per cubic centimeter. A similar resistance was noted in the second patient, who had an acute pustular folliculitis of the legs. The causative organism was a coagulase-positive hemolytic Staph. aureus, sensitive to pencillin in a strength of 20 units per cubic centimeter. The lesions persisted after thirteen days of therapy with penicillin ointment, 10,000 units per gram, and a second test showed that the organisms had become resistant to 500 units of penicillin per cubic centimeter. The facts observed in these 2 patients demonstrate that even massive penicillin therapy may be inadequate and predispose to the development of increased resistance to penicillin when the initial resistance of the organisms to penicillin is relatively high. They also confirm earlier observations [1] that both clinical and laboratory evidence of resistance to penicillin may develop in the course of a few days.

Three patients with chronic impetigo and 1 with long-standing multiple ecthymatous lesions, all due to coagulase-positive hemolytic staphylococci with sensitivity to penicillin in a strength of 4 units per cubic centimeter, were treated. Therapy consisted in administration of penicillin ointment, 3,000 units per gram, and all patients were cured within a ten day period.

The staphylococcic infections of 3 patients showed laboratory evidence of sensitivity to penicillin in dilutions of 6, 8 and 10 units per cubic centimeter, respectively. The first had an infectious eczematoid dermatitis of the face of eight months' duration. The process was arrested temporarily during three previous hospitalizations with the use

of penicillin ointment (500 units per gram), but there was invariably a relapse from seven to fourteen days after therapy was stopped. Culture revealed a coagulase-positive hemolytic Staph. albus, sensitive to penicillin in a strength of 6 units per cubic centimeter. Treatment was instituted with an ointment containing 5,000 units of pencillin per gram, and complete involution occurred after two weeks of therapy. Treatment was then continued for another two weeks to insure permanency of results. The second patient had a subacute infectious eczematoid dermatitis involving the canal, tragus and lobule of the left ear. A coagulase-positive hemolytic Staph. aureus, sensitive to 8 units of penicillin per cubic centimeter, was found on culture. Penicillin ointment, in a strength of 7,500 units per gram, was prescribed, and cure took place in six days. The last patient in the group had a treatment-resistant impetginous and pustular infection of the finger of some thirty days' duration. Culture yielded a coagulase-positive Staph. aureus, sensitive to penicillin in a strength of 10 units per cubic centimeter. Penicillin ointment, in a strength of 10,000 units per gram, was administered, and cure occurred in one week.

The last patient in this group had been hospitalized almost continuously for the preceding eight months because of a treatment-resistant sycosis vulgaris. Three million units of penicillin had been administered intramuscularly in eight separate courses, and penicillin ointment had been used for three weeks without effecting any improvement. On culture a coagulase-positive hemolytic Staph. aureus was found, with sensitivity to penicillin in a strength of 20 units per cubic centimeter. Penicillin ointment in a strength of 100,000 units per gram was used, and cure was accomplished with three days of therapy. In all, treatment was continued for five days, and there was not the slightest evidence of local irritation. The patient was followed for another month, but relapse did not occur.

Treatment with Penicillin Ointment in Conjunction with Intramuscular Injections of Penicillin or with Intramuscular Injections Alone.—Few of the patients reported on in this paper were given penicillin intramuscularly at this station. Many had been so treated, however, during previous hospitalizations, and in general the results were disappointing. Frequently, therapy had been administered without preliminary determination of sensitivity to penicillin, and 5 of these cases will be summarized later. The only obvious indication for intramuscular administration of penicillin in treatment of pyoderma is severe infectious eczematoid dermatitis in a widespread distribution. Furthermore, the causative organisms should be sensitive to penicillin in a concentration of not more than 2 units per cubic centimeter by the filter paper method or, in general, as sensitive as the control Florey strain of Staph. aureus. Two patients with widespread infectious eczematoid dermatitis were

treated with penicillin given intramuscularly, but the organisms were resistant to penicillin in both instances and improvement was not derived from penicillin therapy. Too much reliance should not be placed on intramuscular penicillin therapy, especially when the causative organisms are sensitive to penicillin only in concentrations of 4 or more units per cubic centimeter. This point was demonstrated conclusively by the case of the patient, previously mentioned, who received massive local penicillin therapy. It is also well illustrated by the following case report.

A soldier, aged 32, had severe sycosis of twenty years' duration, with resistance to all previous forms of therapy, including roentgen rays to the point of tolerance and sulfonamide compounds administered both locally and systemically. Culture yielded a coagulase-positive hemolytic Staph. aureus which was sensitive to penicillin in a strength of 10 units per cubic centimeter. Prolonged therapy with penicillin was given, penicillin ointment in a strength of 500 units per gram being supplemented with 40,000 units given intramuscularly every three hours. Two courses of six days each were separated by a six day course of sulfadiazine, 90 grains (5.8 Gm.) daily. Clinical arrest was obtained on this regimen and cultures taken from the normal skin during the next five months did not reveal pathogenic organisms. Nevertheless, a minor folliculopustular relapse ensued six months later, and a pathogenic Staph. aureus was found which was sensitive to penicillin only in a concentration of 100 units per cubic centimeter.

In retrospect, it is probable that organisms (presumably lying dormant in hair follicles) whose growth had been retarded by the penicillin not only had again become active but also had developed an increased resistance to penicillin. Furthermore, on the basis of more recent study, it is apparent that the increased resistance to penicillin was engendered by inadequate doses of the drug. Satisfactory local concentrations of penicillin (as judged by clinical cure) cannot be obtained with the aforementioned regimen of treatment in cases of infections in which there is a sensitivity to penicillin in the strength of 10 units per cubic centimeter.

Penicillin Supplemented by Sulfonamide Therapy.—Rammelkamp and Keefer [2] have stated, on the basis of experimental studies, that penicillin and the sulfonamide compounds may act synergistically in the control of infections. They found that small amounts of penicillin, which alone had no inhibitory effect against staphylococci, would enhance the antistaphylococcus action of sulfathiazole in defibrinated whole blood. Clinical experimentation in cases of pyoderma, however, has shown that when the causative organisms are sensitive to penicillin in a concentration of not more than 2 units per cubic centimeter, local penicillin therapy alone almost invariably accomplishes permanent cure. Accordingly, the only reasonable field of usefulness of combined peni-

2. Rammelkamp, C. H., and Keefer, C. S.: Penicillin: Its Antibacterial Effect in Whole Blood and Serum for the Hemolytic Streptococcus and Staphylococcus Aureus, J. Clin. Investigation **22**:649 (Sept.) 1943.

cillin-sulfonamide therapy would seemingly be in the treatment of infections in which the organisms are sensitive to penicillin only in concentrations of 4 or more units per cubic centimeter. However, since penicillin ordinarily is a more potent antibacterial agent than are the sulfonamide compounds in the control of staphylococcic infections, best results in this type of case should be obtained by adequate concentrations of sulfomamide compounds and by concentrations of penicillin calculated from the results of penicillin-sensitivity tests.

Ten patients with treatment-resistant pyoderma with sensitivity to penicillin in dilutions varying from 4 to 20 units per cubic centimeter were treated with penicillin ointment, 500 units per gram, combined with 5 per cent sulfadiazine. The results were disappointing, and cure did not occur in a single instance. It is to be emphasized, however, that 8 of the 10 patients had previously used sulfadiazine ointment without improvement. Further studies, using increasing concentrations of penicillin with sulfadiazine, are now in progress, and results will be reported at a later date. Increasing local concentrations of sulfadiazine are not being used, because of the tendency to local irritation and secondary infectious eczematoid dermatitis.

In 4 cases it has appeared that two courses of penicillin locally, with an intervening course of sulfadiazine by mouth, have been of value in the management of infections moderately resistant to penicillin. In the aforementioned patient, however, relapse finally ensued, and the necessity of an adequate concentration of penicillin cannot be overstressed. The potential value of the penicillin-sulfadiazine-penicillin sequence has been further confirmed by study of the following case.

A soldier, aged 26, with a noncontributory past history, had a chronic, intermittently infectious, eczematoid dermatitis of the left wrist for six years. Four months before he was admitted to the hospital the lesions again became infected, spread locally and to the right hand and were soon complicated by a severe lymphangitis extending to the right axilla. After temporary improvement the dermatitis relapsed, and the lymphangitis became clinically manifest in both upper extremities. Some 500,000 units of sodium penicillin had been administered intramuscularly without improvement. On the patient's admission to the hospital, a coagulase-positive hemolytic Staph. aureus resistant to penicillin in a strength of 50 units per cubic centimeter was found. The lymphangitis and pyoderma persisted despite continuous soaks, and, accordingly, sulfadiazine was administered, 75 grains (4.8 Gm.) daily for eleven days. The lymphangitis began to recur on the eleventh day of sulfonamide therapy; the organism was restudied and was found to have become sensitive to penicillin in a dilution of 4 units per cubic centimeter. Therapy with penicillin applied locally, in a dosage of 3,000 units per gram of ointment supplemented by 40,000 units administered intramuscularly every three hours, was begun. The lymphangitis and the pyoderma were cured with five days of therapy, a residue of low grade eczematoid dermatitis being left.

Penicillin in Combined Staphylococcic and Streptococcic Pyoderma.—Four patients in the present series had combined hemolytic staphylo-

coccus and streptococcus infections. Three of these had infectious eczematoid dermatitis, and the fourth had ecthyma. In the first 2, the hemolytic staphylococci found were insensitive to 100 and to 2,000 units of penicillin per cubic centimeter, respectively, and penicillin was not used, although the streptococci were sensitive to 1 unit per cubic centimeter. The third patient, with both organisms sensitive to 10 units of penicillin per cubic centimeter, failed to improve with penicillin ointment containing 500 units per gram. The last one, with a severe infectious eczematoid dermatitis, was interesting because of the fact that the infection was largely streptococcic in nature and clinical differentiation of the staphylococcic and streptococcic components was possible. The hemolytic streptococcus was sensitive to 1 unit of penicillin per cubic centimeter while the coagulase-positive, hemolytic staphylococcus was insensitive to 10 units per cubic centimeter. The streptococcic lesions cleared in three days with penicillin ointment in a strength of 500 units per gram, while those due to staphylococci persisted and required potassium permanganate baths and ammoniated mercury for their involution.

Penicillin in Aqueous Solution.—Penicillin has been used occasionally in the form of aqueous solutions, in a strength of 25 to 200 units per cubic centimeter for exudative infectious eczematoid dermatitis. In general, this treatment is not to be recommended, for the amount of penicillin necessary to maintain an adequate concentration in continuous wet compresses is prohibitively large. In addition, the sodium salt may be irritating to the tissues, especially when a superimposed overtreatment or contact dermatitis from other agents has occurred. These points are illustrated by the following case.

A soldier, aged 31, had an infectious eczematoid dermatitis of the hands. Local treatment during a three month period included use of solution of aluminum acetate and ointments of chrysarobin, sulfur and salicylic acid, tar and sulfadiazine, all aggravating the eruption. Penicillin soaks, in a strength of 25 units per cubic centimeter, were then given for a two week period, with considerable aggravation of the eruption and no improvement of the pyoderma. On the patient's admission to the hospital, a severe chemical dermatitis and pyoderma were present. Culture revealed a coagulase-positive hemolytic Staph. aureus sensitive to penicillin in a dilution of 10 units per cubic centimeter. Patch tests with a solution of penicillin and with penicillin ointment elicited negative reactions.

In retrospect, it is apparent not only that the infection was insensitive to sodium penicillin in the concentration used but also that a local irritating effect from the preparation had supervened.

Use of Penicillin in Miscellaneous Conditions.—Penicillin has been of little value against furunculosis, secondarily infected acne or infected sebaceous cysts, whether given topically, intramuscularly or by local injection into circumscribed lesions. Temporary improvement of chronic extensive furunculosis has been followed by complete relapse even when

the organisms are sensitive to penicillin in concentrations not exceeding 1 unit per cubic centimeter. General tonic measures and the use of staphylococcus toxoid are to be preferred. In cases of secondarily infected acute dermatophytosis, penicillin may cause an exacerbation of the lesions, even when the organisms responsible for the secondary infection are sensitive to penicillin. This phenomenon may be due to the action of penicillin on tissues sensitized to the fungi causing the ringworm infection, for it is known that a common antigenic substance is present in all fungi. Personal study of reactions to penicillin has suggested that penicillin contains this common antigen.

Penicillin is useful for secondarily infected eczematous dermatoses, but, as stated [1] before, its effect is solely that of an antibacterial agent. No improvement can be expected in the underlying dermatosis, except so far as the dermatosis has been aggravated by the infection.

Empiric Use of Penicillin Therapy.—The question as to whether or not penicillin therapy should be used empirically in cases of severe cutaneous infections may be answered by the following case reports.

A soldier, aged 23, was hospitalized because of an acute infectious eczematoid dermatitis of the face. A test for sensitivity to penicillin was made, but because of the severity of the infection local and intramuscular penicillin therapy was instituted. The eruption became decidedly worse in the following two days, with the development of diffuse cellulitis of the head and autosensitization, eczematous lesions over the body. Culture revealed a hemolytic Staph. aureus, insensitive to penicillin. Colloid baths, continuous soaks with isotonic solution of sodium chloride and soothing topical measures were then prescribed, with gradual involution taking place over a thirty day period. In this case, the ineffectiveness of penicillin was responsible for a dangerous progression of the infection.

A soldier, aged 19, had been bothered with approximately one hundred furuncular lesions over a period of six months. Penicillin intramuscularly had been given on two occasions, 500,000 units in a five day period two months after the onset and 360,000 units in a three day period two months later. Hot soaks of solution of boric acid were used during both courses of treatment. Temporary improvement occurred after each course of penicillin, but after two weeks a complete relapse supervened. On the patient's admission to the hospital, the furunculosis was present in its original severity. Culture yielded a hemolytic Staph. aureus sensitive to penicillin only in a concentration of 20 units per cubic centimeter. A moderate degree of secondary anemia was found. Permanent arrest was obtained after the use of iron, extract of liver, ultraviolet irradiation, multivitamin capsules and a course of staphylococcus toxoid. In this case it is apparent that penicillin could exert no more than a temporary ameliorative effect with the tissue concentration obtained with intramuscular injections; furthermore, the background of lowered resistance would not be altered.

A soldier, aged 25, had a long-standing, intermittently recurrent, nummular eczema of the distal extremities, on which a secondary infectious eczematoid dermatitis had recently developed. The use of ointment of tar improved the eczema but aggravated the pyoderma, and penicillin soaks, 25 units per cubic centimeter, were used for one month, to a total dosage of approximately 500,000 units. No improvement was obtained, and he was referred to this station. On culture, a coagulase-positive hemolytic Staph. aureus, sensitive to penicillin in a

concentration of 20 units per cubic centimeter, was found. The degree of resistance to penicillin encountered in this patient is a definite contraindication to the use of penicillin intramuscularly or locally in the concentrations used in this case.

A soldier, aged 26, was hospitalized because of a severe infectious eczematoid dermatitis and cellulitis involving the face, neck and scalp. Treatment consisted of continuous wet packs and penicillin administered intramuscularly for nine days, to a total of 960,000 units. Gradual improvement ensued, but because of the persistence of the infection penicillin soaks, in a concentration of 25 to 100 units per cubic centimeter, were applied for a two week period. A total of 600,000 units of penicillin was used but without improvement, and the patient was evacuated to this station. Culture revealed a coagulase-negative hemolytic Staph. aureus, insensitive to penicillin in a concentration of 2,000 units per cubic centimeter, and a hemolytic streptococcus, sensitive to penicillin in a dilution of 1 unit per cubic centimeter. The persistence of this infection was due to the reliance on penicillin for the destruction of an organism which was completely resistant to penicillin. The patient made an uneventful recovery in two weeks with boric acid compresses and 3 per cent ammoniated mercury ointment.

A soldier, aged 43, had been treated for a severe sycosis vulgaris with penicillin intramuscularly, in a total dosage of 2,400,000 units. A severe sensitization reaction to penicillin, consisting of generalized urticaria and angioneurotic edema, then supervened, and penicillin therapy was stopped. On the patient's admission to the hospital, ten days later, the reaction had practically cleared, but the sycosis was unimproved. On culture, a coagulase-negative hemolytic Staph. aureus, insensitive to penicillin in a concentration of 2,000 units per cubic centimeter was found.

This case not only emphasizes the wastage of time and penicillin in a completely penicillin-resistant infection but also brings up the important point that severe reactions may result from the use of penicillin. In a recent study, Cormia, Jacobson and Smith [3] found that severe reactions to penicillin occur in 0.5 per cent of patients given prolonged courses. These reactions included severe urticaria, complicated at times by angioneurotic edema, shock, pulmonary edema and convulsions. Acute syncope and serum-sickness-like syndromes were observed. Various types of erythematovesicular eruptions occurred; in some of these, areas which had been the sites of a previous active dermatophytosis or dermatophytid were involved. It is apparent that the administration of penicillin not only is a time-consuming, exact and expensive procedure but also may be complicated by severe reactions. The careful selection of patients for treatment is therefore of the greatest importance.

LABORATORY CONTROL IN MANAGEMENT OF PYODERMA

The filter paper method, because of its convenience, was used for the determination of sensitivity to penicillin in most of the cases. In this method the test organisms were streaked across a blood agar plate and the control organisms across another. Disks of filter paper, 6 mm. in diameter, were then saturated with varying dilutions of penicillin solu-

3. Cormia, F. E.; Jacobson, L. Y., and Smith, E. L.: Reactions to Penicillin, Bull. U. S. Army M. Dept. **4**:694 (Dec.) 1945.

tion and placed on the plates. The sensitivity or resistance of the organisms was determined by comparing the two plates. A strain of the Florey Staph. aureus, maintained in nutrient broth at room temperature, was used as the control. This organism occasionally developed an increased resistance to penicillin; when this occurred the original degree of sensitivity was restored by passage on a blood agar plate followed by inoculation into fresh broth. From time to time the test solutions of penicillin diminished in potency after standing for more than a week; this difficulty was averted by the use of fresh penicillin solutions for each test.

As the study progressed, it became apparent that there were more variations in the results than were warranted by variations in the control organism. It was found that the amount of penicillin solution absorbed on the filter paper when the edge of the paper was dipped into the solution had a possible range of variation of from 0.002 to 0.004 cubic centimeters. Accordingly, it seemed advisable to check the method against one in which the amounts of penicillin solution used were carefully titrated for each test. The control method was that devised by Cooke.[4] In this method an area 2 by 5 cm. is marked off on the bottom of an agar plate, and then exactly 0.1 cubic centimeter of the test penicillin solution is pipetted evenly over the agar within the marked area and dried quickly in the refrigerator. The organisms to be tested are then streaked across the area, and the inhibition of growth or its absence is noted as usual.

In 20 cases tested by both methods, a rough correlation in the results was observed. The control organism was routinely inhibited by 0.03 unit of pencillin per 0.1 cubic centimeter by the Cooke method and by 2 units per cubic centimeter by the filter paper method. There was, however, a distinct tendency for the results by the filter paper method to assay lower than those by the direct method, the ratio being roughly 3 to 1. While this fact in no way invalidates the conclusions drawn in this paper, it may indicate that the proper dosage of penicillin for local therapy is even higher than is suggested in this report. In the future this difficulty may be avoided by exact titration of the amount of solution used in each test, regardless of the method used. Other factors which must be kept constant are the size of the disk, the depth of the agar in the plate and the temperature and duration of incubation. The number of bacteria in the inoculum, said by Sherwood and her associates[5] to influence the final results, was not considered in the present observations.

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4. Cooke, J. V.: A Simple Clinical Method for the Assay of Penicillin in Body Fluids and for the Testing of Penicillin Sensitivity of Bacteria, J. A. M. A. **127**:445 (Feb. 24) 1945.

5. Sherwood, M. B.; Falco, E. A., and de Beer, E. J.: A Rapid, Quantitative Method for the Determination of Penicillin, Science **99**:247 (March 24) 1944.

COMMENT

The results of the present study suggest that the optimum method of administering penicillin in treatment of cutaneous infections is by topical applications of the substance in a water-soluble ointment base. The ointment has many advantages over solutions, whether used locally or parenterally. It is more economical; the penicillin stays in contact with the affected area for a longer period, and much greater local concentrations of penicillin can be attained by application of the ointment than by intramuscular injections.

The importance of performing a test for sensitivity to penicillin prior to the institution of treatment cannot be overemphasized. The results of the sensitivity test proved to be a valuable guide for the use of penicillin therapy. The concentration of penicillin in the ointment should be varied according to the degree of sensitivity of the causative organisms to penicillin. A strength of 500 units per gram

Strength of Penicillin Ointment to Be Used in Treatment According to Sensitivity of Organisms to Penicillin

Sensitivity of Organism		Strength of Penicillin Units per Gram of Ointment
Filter Paper Method, Units per Cc.	Cooke Method, Units per 0.1 Cc.	
1	0.03 to 0.06	500
2	0.1	1,000
4	0.15	3,000
6	0.2	5,000
8	0.25	7,500
10 to 20	0.3 to 0.6	10,000 to 25,000 (?)
20 to 30	0.6 to 1	25,000 to 50,000 (?)
30 to 50	1 to 2	100,000 (?)

was found satisfactory when the organism was sensitive to penicillin in a concentration not greater than 2 units per cubic centimeter by the filter paper method. Preliminary experiments have shown that when the sensitivity ranges from 4 to 10 units per cubic centimeter cure may occur when the strength of the ointment is sufficiently increased. However, the exact concentrations to be used in a given case will have to be determined by further study. The schedule recommended tentatively for additional clinical investigation is shown in the table.

The routine of treatment consisted of preliminary application of hot boric acid packs for twenty minutes, removal of crusts and opening of pustules, followed by application of the ointment. Treatment was administered twice daily when the organisms were sensitive to 1 to 2 units of penicillin and three times daily when they were sensitive to 4 or more units. In the earlier work[1] penicillin therapy was continued for three to five days after clinical involution took place.

On the basis of the present study, however, it is felt that the length of treatment after involution should be five days in cases of simple pyoderma and up to two weeks in cases of slowly clearing or relapsing infections. In this series, prolongation of therapy has not been followed by an appreciable increase in sensitization reactions.

The frequency of natural resistance of the Staph. aureus to penicillin has not been definitely established. The causative organisms in 22.5 per cent of patients treated in the earlier series [1] were initially resistant to penicillin, while the organisms in an additional 15 per cent became resistant as a result of inadequate penicillin therapy. The high percentage of organisms resistant to penicillin encountered in this series (75 per cent) was thought to be due partly to intrinsic resistance of the organisms, with filtering of the cases through various treatment centers to this station, and partly to developing resistance as a result of previous inadequate penicillin therapy. Analysis of previous treatment disclosed that in some instances short courses of penicillin intramuscularly had been given while in others penicillin was incorporated in an inert type of base, such as cold cream or petrolatum. In an additional group, an inadequate concentration of penicillin, such as 200 units of penicillin per gram of ointment base, was used.

It was impossible to predict the development of resistance to penicillin from the results of initial sensitivity tests. It is probable that resistance is more likely to develop when the organisms are initially sensitive to penicillin in a strength of more than 2 units per cubic centimeter. Increased resistance to penicillin is undoubtedly provoked by inadequate doses regardless of the method of administration. On the basis of former observations [1] and of several cases studied in the present series, there is some suggestion that an intervening course of a sulfonamide compound may alter favorably the response of staphylococcic pyoderma to penicillin; conversely, it is possible that an intervening course of penicillin may affect similarly the reaction of the infection to the sulfonamide compounds.

Resistance of the organisms to penicillin was not of unfavorable prognostic significance so far as cure by other methods of treatment was concerned. The development of resistance to penicillin may be avoided for the most part by an adequate concentration of penicillin in a water-soluble ointment base and by continuation of treatment for at least five days after clinical involution occurs.

Penicillin is a valuable adjunct in the treatment of pyoderma but should be used only in carefully selected cases. Moreover, since many infections do not respond to penicillin, standard methods of treatment often must be used.

SUMMARY

1. Penicillin is a valuable adjunct in the management of treatment-resistant pyoderma.

2. Penicillin should never be administered for pyoderma unless a test for sensitivity to penicillin has been made.

3. The best method of administration of penicillin for pyoderma is by local applications in a water-soluble ointment base.

4. A concentration of 500 units of penicillin per gram of ointment is efficacious when the causative organisms are sensitive to penicillin in a concentration of not more than 2 units per cubic centimeter by the filter paper method and 0.1 unit per 0.1 cubic centimeter by the Cooke method.

5. When the causative organisms are sensitive to penicillin only in concentrations greater than those mentioned in paragraph 4, the amount of penicillin in the ointment should be appropriately increased.

6. Supplementary therapy with sulfonamide compounds has been of limited value in this series.

7. Inadequate dosage and short periods of administration of penicillin are believed to predispose to the development of resistance to penicillin.

ETIOLOGIC CONSIDERATIONS OF KERATOSIS BLENNORRHAGICA

Report of a Case in Which Penicillin Was Used

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SINCE the first case report of keratosis blennorrhagica, by Vidal in 1892, this comparatively rare disease has been discussed thoroughly by a great number of authors.

Half a century of literature based on the pathologic investigation and observation of well over 100 cases has clarified many aspects of the disease and has brought out data and facts which are now generally accepted. Most authors seem to agree today on its morphologic aspects, on its incidence and on its relation to age, to sex and to other gonorrheal complications. However, there is great uncertainty and considerable disagreement concerning the pathogenesis of the disease. While gonorrheal infection is accepted by most of the authors as the primary etiologic factor, there still remain unanswered questions that are open for further inquiry and discussion.

To facilitate such investigation and discussion we wish to restate certain facts already known and to tabulate the data gleaned out of the literature of fifty years. Using as a point of departure the excellent chapter of Buschke and Langer [1] on gonorrheal dermatoses, which covers the literature up to 1926, and Langer's chapter in the *Handbuch*,[2] we have collected reference material on the subject from 1927 to the present.

INCIDENCE

We have found 108 cases of gonorrheal keratosis reported in the literature since 1927. Adding to this number the 57 cases collected by Buschke and Langer, plus our following case report, there have been 166 cases reported in the entire literature to our knowledge. This figure is greatly at variance with the figures of other authors, shown in table 1.

1. Buschke, A., and Langer, E.: Lehrbuch der Gonorrhöe, Berlin, Julius Springer, 1926.

2. Langer, E.: Hautkrankheiten bei Gonorrhöe, in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1930, vol. 22, pt. 2, pp. 40-71.

Our figure of 166 cases does not include the cases reported as keratosis blennorrhagica without gonorrhea or as Reiter's disease with keratosis. We have found 28 such case reports since 1927 and about 34 references in the entire literature. Mastrojanni [3] in 1936 mentioned 10 such cases, including his own. Some of these cases, however, may easily be interpreted as instances of gonorrheal keratosis, in spite of the lack of microscopic and cultural evidence.

According to the present consensus there is no sharp dividing line between the various types of gonorrheal exanthemas and gonorrheal keratosis; some cases reported as instances of hemorrhagic, vesicular, urticarial or other exanthemas may fall into the category of cases of keratosis blennorrhagica. We have to assume, therefore, that these figures are far from representing the actual incidence of keratosis blennorrhagica and other gonorrheal exanthemas, as the number of

TABLE 1.—*Number of Cases of Gonorrheal Keratosis Reported by Various Authors*

Author	Year	Number of Cases
Simpson [22]	1912	20
Haase [66]	1916	30
Keim [69]	1924	59
Buschke and Langer [1]	1926	57
Willmott [184]	1926	65
Millis, E. R.: Urol. & Cutan. Rev. 31 : 418, 1927	1927	70
Scomazzoni [7]	1931	90
Downing [30]	1934	83
Combes, Dietrich and Cohen [26]	1940	93
Rajam and Rangiah [27]	1941	93

unreported cases must be considerable. Nevertheless, we can safely conclude that keratosis blennorrhagica is a rare disease but perhaps not quite so rare as was formerly believed.

Arning and Meyer-Delius [4] found in 4,850 cases of gonorrheal infection 159 cases of arthritis and 6 cases of keratosis. Harrison [5] found 1 case of keratosis in 5,000 cases of gonorrhea. Brown and Hargreaves [6] reported a ratio of 1:7,500. Scomazzoni [7] found 2 cases of keratosis in 11,000 cases of gonorrheal infections, a ratio of 1:5,500.

The age of the patients reported with keratosis blennorrhagica was predominantly in the fourth decade. Many of them were in their

3. Mastrojanni, D.: Contributo allo studio della poliartrite ipercheratosica infettiva, Arch. ital. di dermat., sif. **12**:105, 1936.

4. Arning, E., and Meyer-Delius, H.: Beitrag zur Klinik der gonorrhoischen Hyperkeratosen, Arch. f. Dermat. u. Syph. **108**:3, 1911.

5. Harrison, L. W.: Venereal Disease in General Practice, London, Oxford University Press, 1918.

6. Brown, W., and Hargreaves, H.: A Case of Gonorrheal Keratosis, Brit. J. Dermat. **29**:107, 1917.

7. Scomazzoni, T.: Considerazioni sulla patogenesi della cheratodermia blennorrhagica, Gior. ital. di dermat. e sif. **72**:716, 1931.

twenties, a few in their forties and some in other age groups. Three cases of children 5 to 7 years of age with typical lesions of keratosis were reported; their primary disease was gonorrheal vulvovaginitis (Langer,[2] Louste and Levy-Franckel [8]). The disease mainly affects the male sex, a curious fact never yet explained. We have found 10 cases of keratosis blennorrhagica affecting women (Robert,[9] Levy-Franckel,[10] Isaac,[11] Lees,[12] Buschke and Langer,[13] Beatty,[14] Kristjanssen,[15] Finlay,[16] Wayson [17] and Goldman [18]), a ratio of 1 woman to every 15.3 male patients. Among the patients reported with keratosis without gonorrhea or with Reiter's disease with keratosis 4 were women and 30 were male patients. Of the 25 patients reported since 1927 as having gonorrheal exanthemas without keratosis, 21 were men, 2 were women and 2 were infants.

SYMPTOMATOLOGY AND CLINICAL COURSE

First described by Vidal [19] (1892) in France, Buschke [20] (1899) in Germany, Turnbull and Sequeira [21] (1910) in England and Simpson [22] (1912) in America, the clinical characteristics of keratosis blennorrhagica

8. Louste, A., and Levy-Franckel, A.: Keratose blennorrhagique chez une fiellette de cinq ans, Bull. Soc. franç. de dermat. et syph. **37**:362, 1930.

9. Robert, E.: Contribution a l'étude des troubles trophiques cutanées dans la blennorrhagie, Thesis, Paris, no. 300, 1897.

10. Levy-Franckel, A.: Keratodermie blennorrhagique, Ann. d. mal vén. **13**:385, 1918.

11. Isaac, C. L.: A Case of Keratodermia Blennorrhagica in a Woman, Brit. J. Dermat. **32**:195, 1920.

12. Lees, D.: Keratodermia Blennorrhagica, Edinburgh M. J. **28**:99, 1922.

13. Buschke, A., and Langer, E.: Hyperkeratotische Exantheme bei Gonorrhöe und ihre Beziehungen zur Psoriasis, Dermat. Wchnschr. **76**:145, 1923.

14. Beatty, J.: Symmetrical Hyperkeratosis of Extremities (Keratodermia Blennorrhagica), Brit. M. J. **1**:14, 1927.

15. Kristjanssen, A.: Gonorrhoeische Keratosen, Zentralbl. f. Haut- u. Geschlechtskr. **29**:257, 1929.

16. Finlay, D. E.: Keratodermia Blennorrhagica, Brit. M. J. **1**:979, 1931.

17. Wayson, J. T.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **24**:291 (Sept.) 1931.

18. Goldman, B. A.: Keratodermia Blennorrhagica: Report of Cases, Pennsylvania M. J. **37**:299, 1934.

19. Vidal, E.: Éruption généralisée et symétrique de croûtes cornées avec chute des ongles d'origine blennorrhagique, coincidant avec une polyarthrite de même nature: récidive à la suite d'une nouvelle blennorrhagie deux ans après la guérison de la première maladie, Ann. de dermat. et syph. **4**:3, 1893.

20. Buschke, A.: Ueber Exantheme bei Gonorrhöe, Arch. f. Dermat. u. Syph. **48**:181 and 385, 1899.

21. Sequeira, J. H.: Case of Keratodermie Blennorrhagique, Proc. Roy. Soc. Med. **3**:77, 1909-1910.

22. Simpson, F. E.: Kératodermie blennorrhagique, J. A. M. A. **59**:657 (Aug. 24) 1912.

have been discussed in excellent papers by Arning and Meyer-Delius,[4] Chauffard and Fiessinger,[23] Buschke and Langer,[1] Lees and Percival,[24] Taylor,[25] Combes, Dietrich and Cohen,[26] and Rajam and Rangiah.[27]

The salient clinical points are as follows: Keratosis blennorrhagica is the cutaneous manifestation of a grave systemic disease. The systemic manifestations are always preceded several days, weeks or months by the onset of urethritis, proved gonorrheal in a majority of the cases. Prostatitis and inflammation of the seminal vesicles are also commonly present. Swelling and pain of several joints in succession or simultaneously follow, preceding the onset of cutaneous lesions. The swelling and redness are not severe; however, the pain may be excruciating and the motility of joints limited. Four cases of keratosis without arthritis were reported by Jones,[28] Scholtz,[29] Downing [30] and Morita.[31] A large number of the patients have had a history of several previous or successive attacks of gonorrhea, arthritis and keratosis developing with each relapse or reinfection. In several cases reported as instances of nongonorrheal disease or as Reiter's disease, a history of 1 or more attacks of urethritis associated with inflammation of the adnexa following shortly after intercourse was at least highly suggestive of a latent gonorrheal focus. In some cases the onset of the syndrome followed immediately the passing of sounds or other urethral manipulations in an apparently nongonorrheal patient who, however, had a history of previous gonorrheal infection (Finger,[32] Lewin,[33] Langer,[2] Malherbe,[34]

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23. Chauffard, A., and Fiessinger, N.: Deux cas de kératose blennorrhagique; réproduction expérimentale de la lésion cutanée, Bull. Soc. franç. de dermat. et syph. **20**:162, 1909.

24. Lees, D., and Percival, G. H.: Keratodermia Blennorrhagica, Lancet **2**:1116, 1931.

25. Taylor, N. S.: Keratoderma Blennorhagicum, Brit. J. Dermat. **51**:418, 1939.

26. Combes, F. C.; Dietrich, C., and Cohen, J.: Keratosis Blennorrhagica, J. A. M. A. **114**:2078 (May 25) 1940.

27. Rajam, R. V., and Rangiah, P. N.: Keratodermia Blennorrhagica, Indian M. Gaz. **1**:468, 1941.

28. Jones, T. R. L.: Unusual Case of Hyperkeratosis Blennorrhagica, Brit. M. J. **1**:153, 1929.

29. Scholtz, M.: A Syndrome of Blennorrhagic Keratoderma, Arch. Dermat. & Syph. **15**:165 (Feb.) 1927.

30. Downing, J. G.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **23**:760 (April) 1931; J. A. M. A. **102**:829 (March 17) 1934.

31. Morita, S.: Case of Keratoderma Plantare in a Gonorrhea Case, Jap. J. Dermat. & Urol. **36**:31, 1934.

32. Finger, E.: Purpura rheumatica als Komplication blennorrhagischer processe, Wien. med. Presse **21**:961, 1880.

33. Lewin, G.: Erythema exsudativum multiforme, Charité-Ann. (1876) **3**: 622, 1878.

34. Malherbe: Urethrites a gonocoques recidivantes, arthropathies multiples, troubles trophiques cutanées, cornes, Gaz. méd. de Nantes, 1901, vol. 16, no. 6.

and Sullivan [35]). The onset of the exanthema, which usually follows the onset of arthritis, is sudden and is associated with chills and fever. Within a few days large areas of the skin may be involved, showing lesions in different stages of evolution. The distribution of the cutaneous lesions is symmetric, with a predilection for the feet, soles, ankles and hands, the areas around the involved joints and the genitals. The lesions have been less frequently observed on the scalp, the trunk and the mucous membranes of the mouth. They may be widely disseminated or may be localized only on the extremities (Baermann). A number of cases were reported with localization only on the penis, a clinical picture called "balanitis circinata sicca" (Arning and Meyer-Delius,[4] Jeanselme and Blamontier,[36] Baermann,[37] Chauffard and Fiessinger,[23] Jadassohn,[38] Blumenthal and Sherman,[39] Sherman, Blumenthal and Heidenreich,[40] Gadrat and Morel [41] and Reiss [42]). The typical lesion begins as a pinhead-sized to lentil-sized hard vesicle surrounded with an erythematous halo. It soon becomes a pustule with dry cheesy content. After the pustule breaks open, losing its top, it forms a dirty brown, hard crust with an indurated corneous collar. Interspersed among the lesions occasional papules, hemorrhagic bullae, and erythematous plaques can be observed.

In the later stages of evolution there is an extensive coalescence of the mature lesions forming relief-map-like areas which may involve the whole sole or palm and large areas around the involved joints. These confluent areas have a dusky red and slightly moist base and sharp, slightly raised margins and are covered with dry powdery scales. This picture may predominate from the beginning on the genital and perineal regions with more or less oozing, showing a scarcity of typical vesicles or pustules. The sharp margins, dusky red base and powdery or flaky scales may suggest a resemblance to psoriasis.

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35. Sullivan, S. J.: Cutaneous Eruptions Accompanying Gonorrhea: Report of a Case of Hemorrhagic Exanthema, Urol. & Cutan. Rev. **38**:93, 1934.

36. Jeanselme, E., and Blamontier: Un cas de kératose blennorrhagique strictment localisée au gland, Bull. Soc. franç. de dermat. et syph. **10**:493, 1922.

37. Baermann, G.: Ueber hyperkeratotische Exantheme, Arch. f. Dermat. u. Syph. **69**:363, 1904.

38. Jadassohn, J.: Ueber infectiöse und toxische hämatogene Dermatosen, Berl. klin. Wchnschr. **37**:38, 1904.

39. Blumenthal, F., and Sherman, W. L.: Penile Blennorrhagic Keratoderma with Abortive Course, Am. J. Syph., Gonor. & Ven. Dis. **22**:176, 1938.

40. Sherman, W. L.; Blumenthal, F., and Heidenreich, J: Blennorrhagic Balatiniform Keratoderma, Arch. Dermat. & Syph. **39**:422 (March) 1939.

41. Gadrat, J., and Morel, L.: Gonococcie sévère avec arthropathies multiples, Bull. Soc. franç. de dermat. et syph. **42**:1849, 1935.

42. Reiss: Urethralgonorrhöe, Balanitis gonorrhoica, Arthritis gonorrhoica, Zentralbl. f. Haut- u. Geschlechtskr. **37**:17, 1931.

The toes and fingers show a diffuse, slightly moist, erythematous involvement of the last phalanges, on which firm pinhead-sized vesicles are scattered. These vesicles have a clear waxy content and do not enlarge or become real pustules before they break down. The picture is strongly suggestive of acrodermatitis perstans. The nails become dry and brittle, and may be lifted up from the nail bed by subjacent lesions and heaped-up corneous material.

The scalp, if involved, shows vesicles and papules on erythematous plaques which soon coalesce into moist scaly areas with a predilection for the hairline, a picture which strongly resembles seborrheic dermatitis. In the mouth, the lesions may be localized on the cheeks, on the tongue and especially on the hard and soft palate. These lesions are discrete flat lentil-sized papules with grayish keratotic borders sitting on erythematous bases. Their appearance follows closely the onset of the arthritis, and they disappear within a week or ten days. These oral lesions were reported in the cases of Stanislawski,[43] Frei,[44] Barrett,[45] Guerrieri,[46] Bogrow,[47] Sherman, Blumenthal and Heidenreich,[40] Berman,[48] Genner and Boas,[49] Chambers and Koetter,[50] Epstein [51] and Epstein and Chambers.[52]

According to the present consensus, the nonkeratotic gonorrheal exanthemas do not constitute separate entities. Erythemas, urticarias, erythema-multiforme-like or erythema-nodosum-like, as well as hemorrhagic-bullous lesions, are found simultaneously or successively in many cases, and they are to be considered as different evolutionary

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43. Stanislawski, W.: Ueber einen Fall von gonorrhoischer Urethritis mit Affektion der Gelenke, symmetrischem hornartigen Haut ausschlag und Ausfallen der Nagel, Monatsb. d. Krankh. d. Harn- u. Sex.-Appar. **5**:643, 1900.

44. Frei, W.: Gonorrhoisches Exanthem und Enanthem bei Arthritis gonorrhoica, Zentralbl. f. Haut- u. Geschlechtskr. **4**:323, 1922.

45. Barrett, C. C.: Keratosis Blennorrhagica, Arch. Dermat. & Syph. **22**:627 (Oct.) 1930.

46. Guerrieri, T.: Blenoderma cheractósico, Gior. ital. d. mal. ven. **65**:361, 1924.

47. Bogrow, S. L.: Ueber gonorrhoische Keratosen: Ein Fall von gonorrhoischen Keratosen der Haut und Mundschleimhaut, Arch. f. Dermat. u. Syph. **143**:23, 1923.

48. Berman, L.: Ueber einen Fall von gonorrhoischer Keratose der Haut und Mundschleimhaut, Dermat. Ztschr. **51**:420, 1928.

49. Genner, V., and Boas, H.: Case of Gonorrheal Blennorrhagicum, Arch. Dermat. & Syph. **9**:423 (April) 1924.

50. Chambers, S. O., and Koetter, G. F.: Keratosis Blennorrhagica, Arch. Dermat. & Syph. **27**:411 (March) 1933.

51. Epstein, E.: Hyperpyrexia in the Treatment of Keratoderma Blennorrhagicum, Am. J. Syph., Gonor. & Ven. Dis. **21**:148, 1937.

52. Epstein, E., and Chambers, S. O.: Keratosis Blennorrhagica with Corneal Lesions, Arch. Dermat. & Syph. **36**:1044 (Nov.) 1937.

stages of keratosis blennorrhagica, although actual crusting may not be present (Buschke,[53] Buschke and Langer,[54] Hodara,[55] Combes, Dietrich and Cohen [26] and others).

Involvement of the eyes is not infrequently associated with keratosis blennorhagica, usually as an endogenous and bilateral conjunctivitis which produces a seropurulent, sterile discharge and has a rapid, benign course. Corneal ulcerations (Epstein and Chambers [52]) as well as anterior synechias, iridocyclitis and retinitis have rarely been reported. Other rare complications may be acute glomerular nephritis (Spink and Keefer [56]), hepatitis with hypochromic anemia, general lymphadenopathy, tenosynovitis and bursitis. Endocarditis was rarely observed in this disease (Neiders,[57] Reiss,[58] Sullivan [35] and Welander [59]) and myocarditis was reported only in 1 case to our knowledge (Gadrat and Morel [41]).

The general condition of the patient is usually grave. The temperature is swinging, with daily peaks of between 100 and 102 F. for several weeks. The mental condition of the patient is poor, bordering on melancholia and often on lethargy. Some authors have suggested that this condition is due to the effect of gonococci and their toxins on the cord and the higher centers (Jeanselme,[60] Launois,[61] Jacquet and Ghika [62] and Buschke [53]). However, neurologic examinations do not as a rule reveal any essential changes or abnormalities.

The course of the disease is slow; exacerbations of symptoms referable to joints, eyes and skin are frequent long after the urethritis has cleared. The patient loses weight rapidly and becomes debilitated

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53. Buschke, A.: Ueber universell symmetrische entzündliche Hyperkeratosen auf uro-septischer und arthritischer Basis, Arch. f. Dermat. u. Syph. **113**:223, 1912.

54. Buschke, A., and Langer, E.: Hyperkeratotische Exantheme bei Gonorrhöe und ihre Beziehungen zur Psoriasis, Dermat. Wchnschr. **76**:145, 1923.

55. Hodara, A.: Ein Fall von Gonokokämie und generalisiertem gonorrhoischem Exanthem, Dermat. Wchnschr. **55**:397, 1912.

56. Spink, W. W., and Keefer, C. S.: Renal and Dermatologic Complications of Gonococcus Infections, New England J. Med. **217**:241, 1937.

57. Neiders, K.: Ein Fall von Keratosis gonorrhoica, Dermat. Wchnschr. **1**:751, 1934.

58. Reiss, Gonorrhoische Sepsis, Zentralbl. f. Haut- u. Geschlechtskr. **37**:580, 1931.

59. Welander, E.: Ein Fall von Blennorrhöe, mit Endocarditis und kutanen Manifestationen kompliziert, Monatsh. f. prakt. Dermat. **21**:50, 1895.

60. Jeanselme, E.: Troubles trophiques dans la blennorrhagie, Ann. de dermat. et syph. **6**:525, 1895.

61. Launois, P. E.: Arthropathies récidivantes; amyotrophie généralisée, troubles trophiques multiples d'origine blennorrhagique, Bull. et mém. Soc. méd. d. hôp. de Paris **16**:736, 1899.

62. Jacquet, L., and Ghika: Sur un cas d'arthro-blennorrhagisme avec troubles trophiques, Bull. et mém. Soc. méd. d. hôp. de Paris **14**:93, 1897.

and cachectic; the muscles around the involved joints waste away rapidly. After a course of several months the arthropathies clear up as a rule without leaving any permanent damage, although a few cases of anklyosis have been reported. The involution of the cutaneous lesions is extremely slow, but they heal without leaving any scars. Relapses are not infrequent and are commonly associated with recurrences of gonorrheal adnexal inflammations or reinfections. Death due to intercurrent diseases and cachexia has been reported in about 10 per cent of the cases (Sutton and Sutton [63]).

HISTOPATHOLOGY

The histologic characteristics of keratosis blennorrhagica were studied by Chauffard and Fiessinger,[23] Arning and Meyer-Delius,[4] Buschke and Michael,[64] Baermann,[37] Paschen and Jentz,[65] Haase,[66] Langer,[2] Sobotka [67] and Adamson,[68] and were described in great detail by Keim,[69] Gans,[70] Simpson [22] and Rostenberg and Silver.[71].

The histologic picture is not sharply specialized; it shows similarities with other types of exanthemas, and it varies according to the age and site of the lesions. The earliest manifestation is an exudatory, inflammatory process in the prickle cell layer of the epithelium and papillary and subpapillary layers of the corium. There is vesicle formation in the rete, the contents of these vesicles soon showing polymorphonuclear neutrophils, leukocytes and plasma cells. There is an intracellular and intercellular edema. The tops of the vesicles are formed by one or two layers of squamous cells and a thinning stratum corneum. The base of the vesicle is formed by an increasingly acanthotic, edematous rete. After the vesicle becomes a pustule it breaks open, forming hard, thick parakeratotic crusts. An increased number of mitotic cells

63. Sutton, R. L., and Sutton, R. L., Jr: Diseases of the Skin. St. Louis, C. V. Mosby Company, 1939, p. 969.

64 Buschke, A., and Michael, S.: Zur Kenntnis der hyperkeratotisch-vesulösen Exantheme bei Gonorrhöe, Arch. f. Dermat. u. Syph. **120**:348, 1914.

65. Paschen, E., and Jentz, E.: Ein Beitrag zur Frage der spezifischen Aetiologie gonorrhoischer Exantheme, Med. Klin. **1**:428, 1922.

66. Haase, M.: Keratosis Blennorrhagica, J. Cutan. Dis. **34**:817, 1916.

67. Sobotka: Pustulos-hyperkeratotisches Exanthem bei gonorrhoischer Allgemeinerkrankung, Dermat. Wchnschr. **56**:181, 1913.

68. Adamson, H. G.: Keratodermia Blennorrhagica: Is It a Form of Psoriasis? Brit. J. Dermat. **32**:183, 1920.

69. Keim, H. L.: The Histogenesis of Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **9**:423 (April) 1924.

70. Gans, O.: Histologie der Hautkrankheiten, Berlin, Julius Springer, 1925, vol. 1, p. 348.

71. Rostenberg, A., and Silver, H.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **16**:741 (Dec.) 1927.

can be observed in the squamous layer and over it a parakeratotic stratum corneum of varying thickness, indicating acceleration of the proliferative processes leading to incomplete keratinization (parakeratosis). In the papillary and subpapillary layers there is perivascular infiltration with leukocytes, polymorphonuclears and plasma cells surrounding the distended vessels and the follicles.

PATHOGENESIS

The cause of keratosis blennorrhagica has been the subject of much discussion, especially since Adamson [68] in 1920 and several other authors raised the question of its close relation to arthropathic psoriasis. Its gonorrheal origin has been doubted, denied and confirmed repeatedly. Recently its relation to Reiter's disease emerged as a new point of discussion. Since Wiedmann [72] in 1934 reported the first case of Reiter's syndrome with keratosis several other authors have reported cases with similar interpretations. Kuske [73] even suggested that keratosis blennorrhagica is always due to Reiter's syndrome. Other authors, considering the lack of evidence as to a gonorrheal infection in several reports, doubted the specific gonorrheal character of the disease and, although they admitted a possibile gonorrheal causation, expressed the opinion that other causes may also be responsible (Buschke,[74] Langer,[2] Gottron,[75] Loefgren,[76] Mastrojanni,[3] Baermann,[37] Pawlow and Schindelkroit,[77] Gadrat,[78] Genner and Boas,[49] Scholtz,[29] Silver [79] and Eisner [80]).

Thus one has the opinions of three groups: (1) those denying a gonorrheal causation, (2) those doubting the specific nature of the disease, calling it a syndrome with various causes but with common clinical and pathologic features and (3) those accepting gonorrheal infection as the only primary etiologic factor but (*a*) believing in

72. Wiedmann: Reitersche Erkrankung, Wien. klin. Wchnschr. **47**:1245, 1934.

73. Kuske, H.: Ueber die Hauterscheinungen bei Morbus Reiter, Arch. f. Dermat. u. Syph. **179**:58, 1939.

74. Buschke, A.: Ueber die sog. "Gonorrhoischen Hyperkeratosen" ohne Gonorrhöe, Klin. Wchnschr. **7**:1133, 1928.

75. Gottron: Gonorrhoische Sepsis mit Hautexanthem, Zentralbl. f. Haut- u. Geschlechtskr. **59**:2, 1938.

76. Loefgren, S.: Ein Fall von rezidivierender Keratodermia arthritica, Acta dermat.-venereol. **21**:489, 1940.

77. Pawlow, S., and Schindelkroit, B.: About the So-Called Gonorrheal Keratodermas, Sovet vestnik. venerol. i dermat. **41**:359, 1935.

78. Gadrat, J.: Kératose symétrique et polyarthrite soi-disant blennorrhagique hors de tout gonococcie, Ann. de dermat. et syph. **4**:1040, 1933.

79. Silver, H., in discussion on Feldman.[86]

80. Eisner: Hyperkeratosis (Gonorrhoica?), Zentralbl. f. Haut- u. Geschlechtskr. **22**: 604, 1927.

different pathogenic mechanisms, or (*b*) believing in other accessory and predisposing causes in addition to gonorrheal infection.

The various etiologic interpretations of keratosis blennorrhagica are shown in the outline, which presents the numerous theories concerning the causes of keratosis blennorrhagica and lists the author or authors of each theory.

I. Nongonorrheal causes
   A. Disease without gonorrheal exanthema (Balog [81])
   B. Syphilis (Vidal [19])
   C. Reflex manifestation caused by intraurethral manipulation (Finger [82] and Lewin [83])
   D. Secondary organisms or their toxins (Pawlow and Schindelkroit [77])
   E. Toxic
      1. arsphenamine
      2. arsenic
      3. bromine
      4. lead (Thibierge and Weissenbach [82])
   F. Identical with or closely related to arthropathic pustular psoriasis (Adamson,[68] Jadassohn,[38] Waelsch,[83] Falk,[84] Bogrow,[47] Strandberg and Hedenius,[85] Feldman [86] and Silver [79]
   G. Reiter's disease (Kuske [73])

II. A nonspecific syndrome (may be gonorrheal or nongonorrheal; other causes besides gonorrhea to which it may be due)
   A. Secondary infectious foci or toxins (Strandberg and Hedenius [85] and Pawlow and Schindelkroit [77]
   B. Nongonorrheal foci of infection or toxins (Pawlow and Schindelkroit,[77] Buschke and Langer [13] and Jadassohn [38])
   C. Keratotic diathesis as common factor, with different bacterial or toxic causes (Jadassohn,[38] Adamson,[68] Waelsch,[83] Feldman,[86] Buschke [74] and Langer [2])

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81. Balog, cited by Langer,[2] p. 67.

82. Thibierge and Weissenbach, cited by Scomazzoni.[7]

83. Waelsch, L.: Ueber die Beziehungen zwischen Psoriasis und Gelenkserkrankungen, Arch. f. Dermat. u. Syph. **104**:195 and 453, 1910.

84. Falk, A.: Psoriasis arthropathica (einschliesslich der sog. "hyperkeratotischen Exantheme" bei gonorrhoischen Gelenkerkrankungen), Arch. f. Dermat. u. Syph. **129**:299, 1921.

85. Strandberg, J., and Hedenius, J.: Gonorrheal Keratodermia, Wien. Arch. f. inn. Med. **51**:6, 1919. Strandberg, J.: May Keratodermia Appearing in Connection with Joint Affections of Gonorrhoic or Non-Gonorrhoic Origin Be Regarded as Expression of Parakeratosic Diathesis? Acta dermat.venereol. **11**:70, 1930.

86. Feldman, S.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **27**:889 (May) 1933.

D. Arthropathy, specific or nonspecific, with disposition for keratosis, which may be
   1. familial
   2. endocrine
   3. metabolic (Lojander [87] and Löhe and Rosenfeld [88])

E. Nonspecific
   1. toxic
   2. metastatic
   3. septic (Rostenberg and Silver [71])

F. Reiter's disease (Wiedmann,[72] Kuske,[73] Kruspe,[89] Beck,[90] Postma [91] and Bauer and Engleman [92])

III. Caused by gonorrheal infection

A. Direct causes

1. Lesions arising as the direct effect of gonorrheal organisms *in loco* (Gougerot and Meaux Saint-Marc,[93] Chauffard and Fiessinger,[28] Kiene,[94] Bogrow,[47] Strominger, [95] Simpson and Beeson,[96] Sullivan, Rolnick and White,[97] Lees and Percival,[24] Szathmary [98] and Aust [99])

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87. Lojander, W.: Ueber Keratodermien im Anschluss an Gelenkaffektionen gonorrhoischen und nichtgonorrhoischen Ursprungs, Acta dermat.-venereol. **8**:227, 1927; Ein Fall von Keratodermia arthritica ohne nachweisbare gonorrhoische Infection, ibid. **9**:142, 1928.

88. Löhe, H., and Rosenfeld, H.: Klinische und physiologisch-chemische Untersuchungen über die Hyperkeratosenbildung bei Gonorrhöe und bei Psoriasis pustulosa arthropathica, Dermat. Ztschr. **55**:355, 1929.

89. Kruspe: Zur Aetiologie der Reiterschen Erkrankung, Dermat. Wchnschr. **112**:457, 1941.

90. Beck, F.: Ein Beitrag zur der sog. Spirochaetosis arthritica Reiter, Med. Klin. **33**:1162, 1937.

91. Postma, C.: A Case of Reiter's Disease, Acta dermat.-venereol. **18**:691, 1937.

92. Bauer, W., and Engleman, E. P.: A Syndrome of Unknown Etiology Characterized by Urethritis, Conjunctivitis and Arthritis (So-Called Reiter's Disease), Tr. A. Am. Physicians **57**:307, 1942.

93. Gougerot and Meaux Saint-Marc: Kératose blenorrhagique disséminée; guérison, Ann. d. mal. vén. **7**:818, 1912. Gougerot, H.; Carteaud, A., and Tardieu, A.: Les chancres blennorrhagique, Arch. de dermat. Hôp. St. Louis **1**:201, 1929.

94. Kiene, E.: Ueber die Pathogenese gonorrhoischer Komplikationen, Arch. f. Dermat. u. Syph. **156**:663, 1928.

95. Strominger, L.: Quelques considérations sur la kératose blennorrhagique, J. d'urol. **31**:251, 1931; Sur les exanthèmes gonococciques, Rev. rom. urol. **3**:504, 1936.

96. Simpson, F. E., and Beeson, B. B.: Keratodermie Blennorrhagique, J. A. M. A. **68**:1169 (April 21) 1917.

97. Sullivan, S. J.; Rolnick, H. C., and White, C. J.: Gonorrheal Keratosis: Case Report with Experimental Studies, Illinois M. J. **59**:45, 1931.

98. Szathmary, S.: Beiträge zum Krankheitsbild der Keratosis gonorrhoica, Orvosi hetil. **2**:905, 1928.

99. Aust: Kokkenbefund bei metastatisch-gonorrhoischer Bindehauterkrankung, Ztschr. f. Augenh. **65**:299, 1928.

2. Capillary emboli (Dainow,[100] Photonios and Relias,[101] Bruusgaard and Thjötta,[102] Szathmary [98] and Aust [99])
3. Cocci being destroyed in capillaries, and toxins causing lesions *in loco* (Jadassohn [103])
4. Cocci and their toxins *in loco* together with generalized infection (McDowell [104])
5. Bacteremia, cocci and their toxins in circulation (Buschke and Langer,[1] Jeanselme,[60] Scholtz,[29] Tommasi,[105] Epstein [106] and Thompson [107])
6. Gonorrheal toxemia from gonorrheal foci in glands (Epstein,[106] Scholtz,[29] Haase [66] and Scomazzoni [7])
7. Nervous disturbances (Buschke [74])
8. Trophic disturbances; cocci or toxins causing spinal cord disturbances (Jeanselme,[60] Launois,[61] Jacquet and Ghika,[62] Chauffard and Fiessinger [23] and Lees and Percival [24])
9. Allergy to cocci or to their toxins (Garcia,[108] Scomazzoni,[7] Sherman, Blumenthal and Heidenreich,[40] Tommasi,[105] Rajam and Rangiah,[27] Combes, Dietrich and Cohen,[26] Lees and Percival,[24] Beeson and Ebert [109] and Ohashi [110])

B. Predisposing and accessory causes

1. Secondary infections (Strandberg and Hedenius [85])
2. Idiosyncrasy with keratotic disposition (Photonios and Relias [101])
3. Individual vessel changes (Buschke [74] and DuBois [111])

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100. Dainow, I.: Contribution a l'étude des métastases cutanées de la blennorragie, Inaug. Dissert., Geneva, 1927.

101. Photonios, G., and Relias, A.: Kératodermie blennorrhagique. Reproduction expérimentale des lésions kératodermiques, Bull. Soc. franç. de dermat. et syph. **44**:1775, 1937.

102. Bruusgaard, E., and Thjötta: A Case of Meningitis and Purpura Gonorrhoica, Acta dermat.-venereol. **6**:262, 1925.

103. Jadassohn, J.: Ueber die Komplikationen der Blennorrhöe, Berlin, Urban & Schwarzenberg, 1906.

104. McDowell, J. E.: Keratosis Blennorrhagica or Gonorrheal Keratosis, New York M. J. **115**:518, 1922.

105. Tommasi, L.: Personal communication to the authors, January 1945.

106. Epstein, E.: Pathogenesis of Keratosis Blennorrhagica, Brit. J. Dermat. **51**:428, 1939.

107. Thompson, D. O. B. E.: Gonorrhea, London, Oxford University Press, 1923, p. 231.

108. Garcia, F. M.: Keratodermia Due to Gonorrhea, Prensa med. argent. **20**:739, 1925.

109. Beeson, B. B., and Ebert, M. H.: Keratodermia Blennorrhagica, Arch. Dermat. & Syph. **31**:740 (May) 1935.

110. Ohashi, K.: Keratosis Blennorrhagica, Jap. J. Dermat. **33**:169, 1933.

111. DuBois, C.: Keratoses blennorrhagiques ou dermatitis gonococciques, Acta dermat.-venereol. **5**:1, 1924; cited by Gans.[70]

4. Keratotic disposition: parakeratotic diathesis
   a. Congenital
   b. Acquired
      (*1*) Nervous
      (*2*) Vegetative
      (*3*) Endocrine (Lojander,[87] Strandberg and Hedenius [85] and Lidström [112])
5. Associated keratotic and arthropathic disposition (Lidström [112] and Buschke and Langer [1])
   a. On tuberculous basis (Tommasi [105])
   b. Ether-sulfuric acid increase in joints and skin (Löhe and Rosenfeld [88])
   c. Vitamin A deficiency (Combes and Behrman [113])
6. Mechanical causes:
   a. Inhibition of motion, rest in bed
   b. Increased perspiration, lack of bathing
   c. Compresses, Bier bands (Chauffard and Fiessinger,[23] Buschke [53] and Langer [2])
   d. Injections of vaccine (Olivet [114])
7. Other dermatoses, pyodermic, follicular lesions (Giessing [115])
8. Roentgen irradiations (Oeltze [116])

A definitely nongonorrheal etiologic interpretation could never stand up against the overwhelming contrary evidence. The majority of the authors have accepted the specific gonorrheal pathogenesis, while a smaller group have maintained that in some cases a typical picture of keratosis blennorrhagica may develop with a gonorrheal infection. The main points of controversy are therefore formulated as follows:

I. Is keratosis blennorrhagica a specific entity or is it a syndrome with different causes?

There have been 166 cases reported in the literature in which gonorrhea as the primary cause was not doubted, and only about 34 case reports are known in which the authors did not find any evidence of gonorrheal infection. This ratio is strong evidence in favor of a specific causation.

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112. Lidström, F.: A Contribution to the Question of the Pathogenesis of Gonorrhoic Keratodermia, Acta dermat.-venereol. **10**:457, 1929.

113. Combes, F. C., and Behrman, H. T.: Use of Vitamin A in Keratosis Blennorrhagica, Arch. Dermat. & Syph. **46**:728 (Nov.) 1942.

114. Olivet, J.: Hyperkeratose und Thrombophlebitis bei Gonorrhöe, Med. Klin. **24**:1, 1926.

115. Giessing, H. C.: Keratosis Blennorrhagica, Norsk mag. f. lægevidensk. **2**:97, 1927.

116. Oeltze, F. W.: Ueber Keratosis Gonorrhoica, Arch. f. Dermat. u. Syph. **144**:1, 1923.

Baermann gave the following argument in favor of a specific character of the disease: (*a*) It is constantly associated with gonorrhea. The cutaneous eruption waxes and wanes with the exacerbations and remissions of the gonorrheal infection. (*b*) No similar eruption is found in any other disease or as an idiopathic disease.

In the light of the newer conception of gonorrheal latency some cases reported as nongonorrheal may leave considerable doubt as to their real nonspecific nature. In spite of the failure to observe gonococci the history of previous gonorrheal infections, the presence of urethritis, prostatitis, vesiculitis, arthritis and, often, metastatic conjunctivitis should be strongly suggestive of a latent gonorrheal focus.

Langer analyzed the case reports of Launois,[61] Baermann,[37] Malherbe,[34] Bogrow,[47] Scholtz [29] and Jones [28] with the aforementioned conclusion. However, he as well as Buschke saw patients with typical keratosis but without any evidence of gonorrhea and modified their conception, after much hesitation, in favor of a possible, though rare, nonspecific cause. Langer [2] also pointed out that the patients of Buschke and Langer,[117] Lojander,[87] Löhe and Rosenfeld,[88] Rostenberg and Silver [71] and Eisner [80] had prostatitis and vesiculitis associated with their urethral discharge and showed all the characteristics of gonorrheal keratosis except that gonococci were not observed.

The fact that in some of these cases the disease resembled pustular arthropathic psoriasis made some authors believe in the possibility of a common cause of the two diseases (Adamson,[68] Michael,[118] Lojander,[87] Löhe and Rosenfeld,[88] Buschke and Langer,[117] Flynn,[119] Mitchell,[120] Waelsch [83] and Falk [84]) and for a while the main point of discussion was stated as follows:

II. What is the relation of keratosis blennorrhagica to arthropathic psoriasis?

The question was answered by Keim's [69] excellent work on the pathology of the two diseases. He demonstrated clearly that they are two different entities and his observations were corroborated by other authors (Gans,[70] Haase [66] and Rostenberg and Silver [71]).

Apart from the differences in the general systemic picture and clinical course, the two diseases have also decided histologic differences. Psoriatic lesions do not begin as vesicles, and plasma cells are not seen in the infiltration.

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117. Buschke, A., and Langer, E.: Hyperkeratotische Exantheme bei Gonorrhöe und ihre Beziehungen zur Psoriasis, Dermat. Wchnschr. **76**:145, 1923.

118. Michael, M.: Urethritis non gonorrhoica; Arthritis pseudogonorrhoica, Dermat. Ztschr. **24**:419, 1917.

119. Flynn, J. W.: Keratodermia Blennorrhagicum, M. J. Australia **2**:680, 1927.

120. Mitchell: Blennorrhagic Keratoses; Arthritis; Psoriasis, Arch. Dermat. & Syph. **18**:979 (Dec.) 1928.

Epstein [121] listed the differential diagnostic points between keratosis blennorrhagica and psoriasis as follows:

(*a*) In keratosis blenorrhagica the crusts are firmly attached and are hard to remove.

(*b*) There are no bleeding points after removal of crusts in keratosis blennorrhagica.

(*c*) The lesions begin as vesicles, a process not seen in psoriasis.

(*d*) Arthritis precedes the exanthema, while in psoriasis arthritis is a late symptom.

(*e*) Typical localization of cutaneous lesions on the feet, on the soles and only rarely on the elbows occurs in keratosis blennorrhagica.

(*f*) Large joints are involved chiefly in keratosis blennorrhagica; the arthritis causes no deformities; its onset is acute, and it clears rapidly. In psoriasis the small joints, fingers and toes are involved chiefly; the course is extremely chronic, and deformities are common.

(*g*) Gonorrheal keratosis is associated with a graver general condition.

(*h*) There are differences in the lesions of the mucous membrane and the involvement of the nails.

(*i*) Fever therapy is not successful in the treatment of psoriasis.

Undoubtedly, there are certain morphologic similarities between the two diseases, but according to the present consensus there does not seem to be a deeper connection, and they should be considered as two separate entities.

More recently, cases in which this question might be discussed have been reported only rarely (Feldman [86]). However, in the last ten years a new point of discussion was brought into the literature by European authors, the relation of keratosis blennorrhagica to Reiter's disease.

III. What is the relation of keratosis blennorrhagica to Reiter's disease?

Wiedmann in 1934 was the first to interpret his case of keratosis as a case of Reiter's disease. Up to the present time, 13 cases of keratosis have been reported with a similar interpretation in 10 communications by the following authors: Wiedmann,[72] Naegeli,[122] Kuske,[73] Kruspe,[89] Beck,[90] Postma,[91] Bauer and Engleman [92] and Lever and Crawford.[123]

Reiter's disease, which was first reported by Reiter [124] in 1916 as a spirochetal infection, is actually a syndrome of urethritis, conjunctivitis and arthritis in which gonococci or micro-organisms cannot be demon-

121. Epstein, E.: Differential Diagnosis of Keratosis Blennorrhagica and Psoriasis Arthropathica, Arch. Dermat. & Syph. **40**:547 (Oct.) 1930.

122. Naegeli, O.: Morbus Reiter mit Hautexanthem, Schweiz. med. Wchnschr. **67**:63, 1937; **68**:793, 1938.

123. Lever, W. F., and Crawford, G. M.: Keratosis Blennorrhagica Without Gonorrhea (Reiter's Disease?), Arch. Dermat. & Syph. **49**:389 (June) 1944.

124. Reiter, H.: Ueber eine bisher unbekannte Spirochaeten Infektion (Spirochaetosis arthritica), Deutsche med. Wchnschr. **42**:1529, 1916.

strated. According to Lever and Crawford,[123] 47 cases were reported in 25 communications, including their own, in 13 of which it was associated with keratotic cutaneous lesions. However, the existence of Reiter's disease as an entity has not yet been proved beyond doubt. The case reports are somewhat conflicting; in some the bacterial studies did not seem adequate to exclude the presence of a gonorrheal infection and in others the history of the patient and some clinical observations strongly suggested the possibility of a latent gonorrhea (3 cases reported by Kuske,[73] 2 cases by Foerster [125]).

However, there remain about a score of case reports of keratosis blennorrhagica in the literature with sufficient evidence to exclude gonorrhea, a number small enough in comparison with the number of cases with a definitely or suspectedly gonorrheal origin to raise serious doubts about the specific nature of keratosis blennorrhagica. While it may not be possible to give a satisfactory explanation of the relation of this small number of cases of nongonorrheal keratosis to the number of cases of gonorrheal keratosis, either by assuming that they are due to an undemonstrable latent gonorrheal focus or by classifying them as psoriasis, we can safely conclude that the majority of evidence as well as the majority of authors favor a specific gonorrheal causation of keratosis blennorrhagica.

In the majority of cases the complement fixation test for gonorrhea elicited a positive reaction. However, owing to the numerous negative results in cases of evidently gonorrheal keratosis and to the occasional reports of false positive reactions, the reliability of this test has been questionable, and it has not been used by many authors.

Even though gonorrheal infection is accepted as the specific cause, the actual pathogenesis of the disease is interpreted differently, leading to some controversy among the authors. The main point of discussion can be formulated as follows:

IV. Are the cutaneous, synovial and conjunctival affections of keratosis blennorrhagica caused by the presence of the Neisserian organisms in loco, or by toxic, allergic, trophic or other factors?

The advocates of the "direct effect" conception offer mainly the argument that the gonococci have been demonstrated in the lesions in some patients and that, if their toxins are responsible, the cocci must be present *in loco* because they liberate their endotoxins only while in the process of disintegration.

Contrary to this, the toxic-allergic interpretation holds that the gonococci, because of their biologic properties, cannot vegetate in the skin

125. Foerster, R.: Zwei Faelle von Reiterscher Erkrankung, Med. Welt **7**: 700, 1933.

and are also quickly destroyed in the blood. Furthermore, the organisms have been demonstrated in the lesions as well as in the blood only on rare occasions.

The number of case reports of positive evidence of gonoccocci in the cutaneous lesions of keratosis blennorrhagica collected from the literature by most authors has numbered less than a half dozen. Careful search of the literature, however, yields a much higher number.[126] To obtain complete bacteriologic data on the disease, we have collected the instances of gonococci in the blood,[127] joints [128] and conjunctivas [129] in all types of gonorrheal exanthemas, as shown in tables 2 and 3.

While not all the positive observations of gonococci are entirely convincing in the reports of the authors listed in tables 2 and 3, the majority of them must be considered reliable. For instance, Roark [127b] was not convinced that his blood culture contained typical gonococci.

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126. (*a*) Bulkin, A.: Ein Fall von Keratosis blennorrhagica, Vestnik. dermat. **5**:2, 1927. (*b*) Gager, E. C.: Keratodermia Blennorrhagica, J. A. M. A. **78**:941 (April 1) 1922. (*c*) Wadsack, E.: Ein gonorrhoisches Exanthem, Berl. klin. Wchnschr. **43**:966, 1906. (*d*) Campbell, J. R., cited by Sutton, R. L.: Diseases of the Skin, ed. 5, St. Louis, C. V. Mosby Company, 1923, p. 438. (*e*) Barrett, C. C.: Keratoderma Blennorrhagicum, Arch. Dermat. & Syph. **22**:627 (Oct.) 1930. (*f*) Fuhs: Acrodermatitis continua mit chronischer deformierender Polyarthritis, Zentralbl. f. f. Haut- u. Geschlechtskr. **63**:409, 1940. (*g*) Portugal, H.; Cunha, and Machado: Ceratodermia blennorrhagica, Ann. brasil. de dermat. **13**:55, 1938. (*h*) Cole, H. N., and Driver, J. R.: Keratoderma Blennorrhagica, Arch. Dermat. & Syph. **19**:1025 (June) 1929. (*i*) Hansteen, E. H.: Keratosis Gonorrhoica, Internat. Clin. **4**:62, 1927. Dubois.[111] Dainow.[100] Photonios and Relias.[101] Strominger.[95] Combes and Behrman.[113] Scholtz.[29] Szathmary.[98]

127. (a) Jenkins, J. A.: Gonococcal Septicaemia, Brit. M. J. **1**:641, 1922. (*b*) Roark, B. H.: Blennorrhagic Keratosis, J. A. M. A. **59**:2039 (Dec. 7) 1912. (*c*) Massini: Ueber gonorrhoische Sepsis, Ztschr. f. klin. Med. **83**:1, 1918. (*d*) O'Brien, T. J., and Bancker, E.: Gonococcus Sepsis, New England J. Med. **198**:184, 1928. (*e*) Hazel, O. G., and Snow, W. B.: Gonococcic Septicemia with Purpura and Arthritis Successfully Treated by Hyperthermia, J. A. M. A. **109**:1275 (Oct. 16) 1937. (*f*) Kerl: Gonokokkenexantheme, Zentralbl. f. Haut- u. Geschlechtskr. **49**:587, 1934. (*g*) Friedberg, C. K.: Gonococcemia with Recovery, Am. J. M. Sc. **188**:271, 1934. (*h*) Wiedmann, A.: Beiträge zur Pathologie der Gefässerkrankungen der Haut, Dermat. Wchnschr. **98**:541, 1934. (*i*) Wheeler, G. W., and Cornell, N. W.: Gonorrheal Bacteremia in a Woman, with Apparent Cure by Surgical Intervention, J. A. M. A. **94**:1568 (May 17) 1930. (*j*) Chevalier, P.; Levy-Bruehl, and Bourgeois: Purpura généralise chronique et presque apyretique d'origine gonococcique, Bull. et mém. Soc. méd. d. hôp. de Paris **1**:30, 1927. Hodara.[55] Chauffard and Fiessinger.[23] Dainow.[100] Bruusgaard and Thjötta.[102]

128. (*a*) Bejarano, J., and Orbaneja, J. G.: Contribution à l'étude des syndromes cutanes articulaires, Ann. de dermat. et syph. **6**:994, 1935. (*b*) Jobst: Arthritis Gonorrhoica, Gyógyászat **68**:365, 1928. Fuhs.[126] Strominger.[95]

129. Stewart, W. M.: A'propos d'un cas de kératose gonococcique, Bull. Soc. franç. de dermat. et syph. **47**:160, 1940. Aust.[99]

Portugal, Cunha and Machado [126g] gave no details of the methods and circumstances by which "occasional gonococci" were demonstrated in the cutaneous lesions. On the other hand, in Hodara's case,[55] the positive evidence was obtained from erythematous lesions which later became keratotic.

TABLE 2.—*Positive Evidence of Gonococci in Typical Cases of Keratosis Blennorrhagica*

Skin	By culture or smear	Bulkin [126a]; Gager [126b]; Wadsack [126c]; Campbell [126d]; Barrett [126e]; DuBois [111]; Dainow [100]; Fuhs [126f]; Portugal, Cunha and Machado [126g]; Photonios and Relias [101]; Strominger [95]; Cole and Driver [126h]; Combes and Behrman [113]; Hansteen [126i]; Scholtz [29]
	By histologic examination	Szathmary [98]; Bulkin [126a]
Joints	By culture or smear	Fuhs [126f]; Strominger [95]; Bejarano and Orbaneja [128a]
Eye	By smear	Stewart [129]
	By histologic examination	Aust[99]; previous case referred to by Aust [99]
Blood	By culture or smear	Hodara [55]; Chauffard and Flessinger [28]; Jenkins [127a]; Dainow [100]; Roark [127b]

TABLE 3.—*Positive Evidence of Gonococcus in Nonkeratotic Gonorrheal Exanthemas*

Skin	By culture or smear	Löhe [130a] (herpetic); Chevalier, Levy-Bruehl and Bourgeois [127j] (purpura); Dorner [130b] (erythema); Siegel [130c] (hemorrhagic-pustular); Hodara [55] (erythema); Wolfram [130d] (vesiculopustular); Nitto and Yoshihiro [130e]; Kerl [127f] (pustules); Henning [130f] (vesicles); Pugh [130g] (abscesses)
	By histologic examination	Bruusgaard and Thjötta [102] (in precapillaries of skin and endothelium); Itchikawa and Ohmori [130h] (erythema-multiforme-like); Paschen and Jentz [65] (hemorrhagic-bullous)
Joints	By culture or smear	Jobst [128b] (in 12 cases)
Blood	By culture or smear	Bruusgaard and Thjötta [102]; Massini [127c]; O'Brien and Bancker [127d]; Hazel and Snow [127e]; Kerl [127f] (2 cases); Friedberg [127g] (3 cases); Wiedmann [127h]; Wheeler and Cornell [127i] (7 cases); Chevalier, Levy-Bruehl and Bourgeois [127j]
Liquor spinalis	By smear from spinal fluid in case of gonorrheal septicemia	Decrop, G.: Bull. Soc. franç. de dermat. et syph. **44**: 461, 1937
Heart	By culture from tricuspid and mitral valves after death	Brunet [131]

Seventeen positive observations of gonococci in 166 case reports amounts to about 10 per cent positive bacterial evidence as to the presence of gonococci in the keratotic cutaneous lesions.

Such a high percentage, never before reported by any other authors, should establish beyond doubt the immediate role of the Neisserian organism in the pathogenesis of gonorrheal keratosis. If we add the

80 case reports of nonkeratotic gonorrheal dermatoses and their 13 positive bacterial showings [130] to the cited figures, the percentage of positive observations of gonococci in all types of gonorrheal lesions of the skin is 12.2 per cent.

In contrast to this relatively high percentage, the cultures of the blood only rarely yield gonococci, not only in typical cases of keratosis blennorrhagica but in cases of all types of systemic gonorrheal infections. Even in the severest gonorrheal septicemias, gonococci can rarely be cultured from the blood, probably because they are killed rapidly by its bactericidal properties. Brunet [131] cultured gonococci from the mitral and tricuspid valves of the heart after death of a patient in whose blood he had not been able to demonstrate them with repeated cultures, in spite of the severe septicemic condition which eventually resulted in the patient's death.

Similarly, in the fluid obtained by puncture of joints in gonorrheal arthritis, bacterial evidence is rarely demonstrated. Jadassohn [103] attributed this to the following reasons: 1. The cocci vegetate only in the synovial membrane and do not get into the cavity. 2. If they reach the cavity they are quickly destroyed by the synovial fluid. 3. They may get into the cavity very early or very late in the course of the disease.

The synovial fluids in which gonococci are found have lower bactericidal properties than the blood, whereas a sterile synovial fluid has the same bactericidal capacity as the blood, according to Spink and Keefer.[56] The gonococci are quickly destroyed in the synovial fluid, and are never found after the sixth day.

Jobst,[128b] who reported 12 positive observations in cases of gonorrheal arthritis, attributed the gonorrheal condition of the joints to a disposition created by precurrent tuberculosis, an opinion which is shared by Tommasi [105] and others. Jobst found 5 per cent gonorrheal arthritis

130. (*a*) Löhe, H.: Ueber einen Fall von herpetiformen, gonorrhoischem Exanthem, Dermat. Ztschr. **15**:475, 1908; Psoriasis pustulosa, Zentralbl. f. Haut- u. Geschlechtskr. **28**:416, 1929. (*b*) Dorner, L.: Ueber Gonokokkensepsis, Deutsche med. Wchnschr. **49**:1549, 1923. (*c*) Siegel, L. A.: A Case of Gonococcus Septicemia, Bull. Buffalo Gen. Hosp. **3**:66, 1925. (*d*) Wolfram: Vesiculopustuloes-hämorrhagisches Gonokokkenexanthem, Zentralbl. f. Haut- u. Geschlechtskr. **59**:381, 1938. (*e*) Nitto, S., and Yoshihiro, I.: A Case of Gonorrheal Exanthema, Jap. J. Dermat. **41**:111, 1937. (*f*) Henning, L.: Gonorrhoische Hautaffektion beim Säugling, Dermat. Wchnschr. **92**:96, 1931. (*g*) Pugh, W. S.: Skin Complications of Gonorrhea, Am. Med. **36**:126, 1930. (*h*) Itchikawa, T., and Ohmori, S.: Gonococcus Exanthema, Jap. J. Dermat. **34**:511, 1933. Chevalier, Levy-Bruehl and Bourgeois.[127j] Kerl.[127f] Hodara.[55] Bruusgaard and Thjötta.[102] Paschen-Jentz.[65]

131. Brunet, W. M.: Gonococcal Endocarditis, Am. J. Syph. **23**:207, 1939.

instead of the usual 2 per cent among the miners of Pécs, Hungary, where conditions were poor and the rate for tuberculosis was extremely high.

In only 1 case of metastatic conjunctivitis could gonococci be demonstrated in the seropurulent discharge of the conjunctiva (Stewart [129]). Aust [99] in 1928 demonstrated gonococci in the biopsy specimen taken from the bulbar conjunctiva of a patient suffering with endogenous conjunctivitis, the second such histologic observation, according to his statement.

Further evidence in favor of the "direct effect" conceptions may be seen in the results of the following experiments: In keratotic patients of Chauffard and Fiessinger [23] and Sullivan, Rolnick and White [97] new keratotic lesions were produced by inoculating intact sites on the skin with the scrapings of old lesions. Similar lesions developed on the arms of the patients of Szathmary [98] and Scomazzoni [7] after inoculation with pus of a urethral discharge containing gonococci. Lees and Percival [24] reported the same results with cultures of gonococci. Photonios and Relias [101] not only produced new lesions by inoculating scrapings of old lesions containing gonococci but also could demonstrate the cocci in the reinoculated lesions.

In support of the toxic-allergic interpretation, equally strong arguments have been brought forth. Epstein [106] listed his reasons for a toxic interpretation as follows: (1) rarity of evidence of gonococci in lesions; (2) symmetry of lesions; (3) involvement of mucosae; (4) sterile, toxic conjunctivitis; (5) localization; (6) clearing of lesions with the cure of infectious foci in the adnexa; (7) uselessness of local applications, and (8) coexistence of urethritis and arthritis with the cutaneous lesions.

Scholtz [29] reported that injections of gonococcus vaccine caused new showers of cutaneous eruption. Olivet [114] noticed that new keratotic lesions developed at the sites of injections of gonococcus vaccine. In 1 of their patients, Buschke and Langer [1] observed the reddening and flare-up of lesions after intravenous administrations of gonococcus vaccine. Scomazzoni [7] and others reported cases in which the onset of keratosis occurred after injections of vaccine in subjects with long histories of gonorrhea.

We may add that the general picture of keratosis blennorrhagica is not that of an acute septicemia (Kiene [94]); the arthritis is rarely the phlegmonous, ankylosing variety but is rather a benign seropurulent exudatory type, and the cutaneous lesions are not those of the bacterial-pyodermic dermatoses, but resemble more a chronic toxic-allergic process. The symmetry, appearance and localization of keratoses on the extremities and the condition of the nails may justly suggest toxic-trophic disturbances, an interpretation of Jeanselme,[60] Jacquet and Ghika [62] and others.

Recently the more functional allergic conception has come into the foreground. Proponents of this concept have expressed the belief that the gonococci or their toxins affect the neurovegetative-endocrine balance, causing colloidal disturbances in the cells, a tissular shock leading to sensitization of certain portions of the skin (Garcia [108] and Scomazzoni [7]).

While some aspects of the disease may fit one or the other of these interpretations well, not all the cases nor all of their features can be sufficiently explained by any single "cause." Neither could we obtain a satisfactory explanation by simply adding one cause to another or by the supposition of additional predisposing causes, as a strictly morphologic approach would attempt further clarification.

It is safe to say that one is dealing here with a complex functional disturbance of the whole organism, the magnitude and gravity of which are not in proportion to the extent and duration of the bacterial invasion or of a toxic saturation.

While the physiopathologic allergic interpretation seems to give a broader understanding of this as well as of many other diseases, it is still difficult to explain the total picture of gonorrheal keratosis by the sensitization of only certain portions of the skin, joints and conjunctivas by the cocci or toxins, either directly or through a more general disturbance in the nervous system and the neurovegetative-endocrine systems.

The process, as most authors agree, begins with the invasion of the circulatory system by gonococci, most probably from an adnexal abscess which erodes into the blood stream. The curious fact that chiefly men are affected by keratosis blennorhagica or by other systemic manifestations of gonorrhea is difficult to understand. This may be explained, perhaps, by the greater likelihood of abscesses forming and breaking into vessels of the interstitium in the male adnexal organs, owing to their anatomic structural properties.

Invasion of the circulatory system by gonococci is not likely to be a rare occurrence if one considers the high incidence (2 per cent) of gonorrheal arthritis and the frequent general symptoms, such as chills and fever, in exacerbations of prostatitis and vesiculitis. It is extremely probable that in many gonorrheal infections such an invasion occurs repeatedly and may well lead to an allergic sensitization, the disintegration products of gonococci acting as allergens. It may be of some significance that in most cases keratosis blennorrhagica develops in the fourth decade, usually after a protracted or a repeated attack of gonorrhea. The pus discharged into the blood stream is carried to the various organs as small emboli, according to Hodara,[55] Massini,[127c] Bruusgaard and Thjötta [102] and others. These emboli contain cocci of different virulence and in various stages of disintegration. Caught in the small precapillaries, these emboli and cocci break down quickly, all evidence

pointing toward the fact that gonococci cannot vegetate in the blood or tissues because of their biologic properties and the gonococcidal properties of the blood and tissue fluids (Friedberg,[127g] Wheeler and Cornell,[127i] Kiene,[94] Tommasi [105] and others).

According to the virulence of the cocci and the constitution of the patient, the result of such an invasion may range from slight malaise with no apparent consequences to an acute and grave septicemia associated with endocarditis, arthritis, meningitis and hemorrhagic-bullous, pustular and erythema-nodosum-like cutaneous lesions. For true gonococcic septicemia a mortality of 93 per cent has been reported by Bakst, Foley and Lamb.[132] In gonococcic septicemia allergic manifestations due to previous sensitization may be present although not predominant; however, bacterial-toxic factors stand in the foreground and the course is rapid and severe.

In typical keratosis blennorrhagica the invasion by gonococci may produce pathologic changes in the organism attributable directly to the presence of gonococci *in loco*. This stage does not last long, owing to the rapid disintegration of the invading organism, and it rarely leads to true septicemia (Kiene [94]). The ensuing long illness and the grave general condition of the patient cannot be explained entirely, therefore, by bacterial and toxic causes. The extent and duration of the symptoms are certainly out of proportion to a possible, even if repeated, small scale bacterial infiltration, or to toxic causes originating from the primary focus. The presence of secondary organisms as the cause is highly doubtful, as they have never been demonstrated during the extremely long course of keratosis blennorrhagica. Neither does a piecemeal sensitization of certain tissues and portions of the skin gave a plausible explanation for the whole picture of the disease. This picture suggests that we are dealing here primarily not with a skin problem but with a hyperreactive organism (in the sense of pleoergy of von Groer) sensitized by previous attacks of gonococci to such a degree that the repeated presence, no matter how small, of the gonococci in the system elicits an organismal reaction far beyond that which would be adequate to cope with the actual infection, a quasidesperate reaction in which the organism spends itself and perhaps breaks down completely.

Thus one observes the rapid pulse, the excessive perspiration and the continued swinging temperature without any bacterial evidence to account for these violent reactions. In the skin the reaction is the exudative-vascular type characterized by an acceleration of the proliferative processes and by the heaping up of immense amounts of corneous material and finally resulting in a broken-down erythrodermic skin.

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132. Bakst, H.; Foley, J. A., and Lamb, M.: Gonorrheal Septicaemia and Erythema Nodosum, Ann. Int. Med. **9**:970, 1935.

133. Footnote deleted by the authors.

Furthermore, one can observe the mental attitude of utter defeat, the cachexia and the wasting away of the body without microscopic and serologic examinations revealing sufficient reasons to explain them.

A disease implies not only morphologic tissular change and damage caused directly by the pathogenic agent but also a functional readjustment of the total organism in response to the presence of such an agent, proportionate to it and to the changes caused by it. May not the reaction of the organism to a sensitizing agent be so extreme that, instead of reestablishing an equilibrium after the agent is neutralized, it continues to react with an intensity which leads to exhaustion and perhaps to a breakdown of function ?

TREATMENT

The local treatment of the cutaneous lesions seems to be of little value as long as the primary foci in the glands are not cured. For this reason some authors have advocated operative drainage of the prostate gland and the seminal vesicles. Taylor [25] reported favorable results with local applications of elastoplast, which he left on for seven to eleven days.

In the general management of the disease the following treatments have been used with some benefit: (1) autogenous vaccines, by Scholtz [29]; (2) sulfonamide compounds; (3) 1 per cent solution of merbromin intravenously, by Willmott [134]; (4) iodine in large doses, by Morita [31]; (5) neoarsphenamine, by Lojander [87]; (6) massive doses of vitamin A, by Combes and Behrman [113] and (7) hyperpyrexia by typhoid vaccine or by hypertherm, by Willmott,[134] Hazel and Snow,[127e] Epstein and Chambers [52] and Combes, Dietrich and Cohen.[26]

As general supportive measures, infusions, high caloric diet, vitamins and insulin have been recommended.

REPORT OF A CASE

A 25 year old soldier was admitted to the hospital on Oct. 24, 1944 with an acute gonorrheal urethritis. After receiving 100,000 units of penicillin he was discharged to duty, but the urethral discharge recurred after a few days. On November 6 he complained of pain and swelling in the right great toe, and on November 9 an oozing batwing-shaped erythematous lesion developed in the crotch, and he was readmitted to the hospital on November 13.

He had contracted gonorrhea two years previously; otherwise his history was noncontributory. His last sexual conact was allegedly on October 20.

After readmission on November 13 he received 200,000 units of penicillin. He also was given sulfadiazine, 1 Gm. every six hours for four days. On November 15 bilateral catarrhal conjunctivitis developed. On November 16 his temperature was 99 F. and thereafter followed a swinging course with daily peaks of 100 F., reaching 102 F. on December 27 and then slowly abating. It returned to normal on Feb. 1, 1945 and remained so thereafter.

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134. Willmott, C. B.: "Kératodermie Blennorrhagique" (Vidal), Arch. Dermat. & Syph. **13**:17 (Jan.) 1926.

Penicillin therapy was continued from November 19, with daily doses of 200,000 units, to Dec. 12, 1944. The patient received a total of 5,000,000 units without appreciable results, except for the clearing of the urethral discharge on about November 25.

On November 23 the metacarpophalangeal joint of the left fourth finger, the left knee and the left temporomandibular joints became swollen and extremely painful. On November 25 he complained of pain in the right knee joint; several days later swelling of this joint was noticeable.

The dermatitis of the crotch did not improve in spite of the continued application of hot compresses. Suddenly, on November 27, an erythematous and purpuric exanthema developed, on both feet and hands, which rapidly became

Fig. 1.—Keratosis blennorrhagica on the eighth day of the eruption. Observe the diffuse hyperemia of the right heel and the tendency of the lesions to occur in groups.

pustular and extremely firm to the touch. Two days later papular lesions were discovered on the hard and the soft palate, and spreading of the exanthema, which later showed a strong resemblance to hyperacute monilial dermatophytosis, was noted on both ankles, legs and buttocks and in the genital region. On December 1 lesions were also discovered on the scalp.

Description of Lesions.—After the initial erythematous purpuric stage, the feet, legs, hands and buttocks showed pinhead-sized to bean-sized discrete vesicles which rapidly became pustules. The pustules broke open, revealing scanty cheesy contents, and they developed grayish keratotic caps with dirty brown crusts. In their further evolution, these lesions became confluent, sitting on erythematous, dusky red bases involving large areas of the soles, feet and, later, both knees

and buttocks. These dusky red, slightly moist areas resembled relief maps and in the final stages were covered with adherent, dry, powdery scales and crusts and on their fringes showed torn and loose horny masses.

The genitals were involved in a batwing-shaped, confluent and freely oozing, erythematous rash which later became dry, dusky red and covered with powdery scales. The prepuse could not be retracted owing to balanitis and oozing dermatitis of the outer surface of the prepuce.

The scalp showed a similar picture, especially on the hair line, and also some vesicles and pustules. Later, the lesions of the scalp strongly resembled seborrhea and also psoriasis.

Fig. 2.—Eruption of keratosis blennorrhagica on the fifteenth day; eczematoid areas on the hands.

On the fingers, involving all the last phalanges, moist erythema was noted on which occasional pinhead-sized transparent vesicles were scattered, resembling acrodermatitis continua. These lesions also assumed later the dry, dusky red aspect. The nails of the fingers and toes gradually became opaque and brittle, and they were raised up from the nail beds by heaped-up material under them.

The hard and the soft palate showed discrete, flat papules with keratotic, grayish rings sitting on erythematous bases suggesting an iris design. These later lesions disappeared on December 24, at which time the temporomandibular joint and the right great toe were also healed.

Laboratory Data.—On the patient's admission to the hospital, the urethral smear was positive for gonococci. The sedimentation rate of the blood by the Wintrobe method was 46 mm. per hour. During the patient's stay in the hospital his erythrocytes ranged from 4,200,000 to 5,250,000; his leukocytes, from 10,000 to 13,150; his polymorphonuclears, from 72 to 84 per cent, and his lymphocytes, from 26 to 27 per cent. His hemoglobin remained approximately 80 per cent. The Kahn reaction of the blood was negative. Results of repeated urinalyses

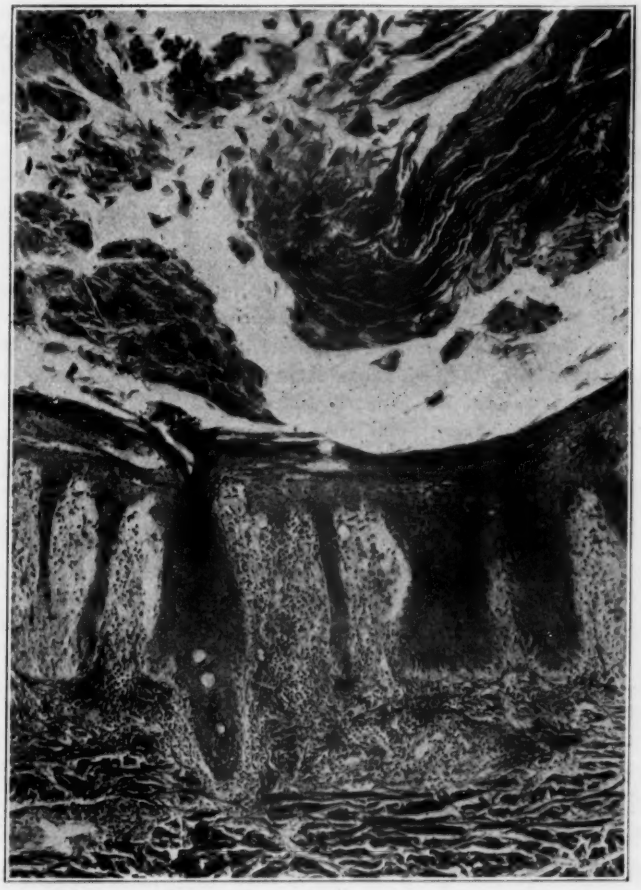

Fig. 3.—Photomicrograph of biopsy specimen from the dorsal surface of the left foot on the tenth day of the exanthema. Note the enormous acanthosis, the hyperkeratosis and the parakeratosis as well as the papillary and subpapillary infiltration with leukocytes. Hematoxylin and eosin; × 60.

were normal. Between November 29 and December 11 repeated urethral smears and cultures of the blood were negative for gonococci. The culture of seropurulent fluid aspirated from the left knee joint on November 29 showed merely occasional staphylococci. Smears and cultures from the cutaneous lesions on the feet disclosed no gonococci but occasional staphylococci. Cultures from the lesions in the mouth were negative for Corynebacterium diphtheriae, and smears from the same

lesions revealed no Vincent's organisms. Smears and cultures from the bilateral conjunctival seropurulent exudates were also negative for pathogens. Roentgenograms showed the involved joints to be normal. The spinal fluid gave a negative serologic reaction, a cell count within normal range, a normal protein content and normal colloidal gold curve.

Biopsy Report.—Biopsy of a specimen from cutaneous lesions of the dorsal surface of the right foot on December 6 and examined by an army general medical laboratory was reported as follows:

"The intraepidermal space, noted grossly, is formed between layers of a parakeratotic and edematous epithelium. The intercellular spaces around the edges of this bleb form irregular crevices which are filled with polymorphonuclear leukocytes. There are moderate acanthosis and hyperplasia of the subjacent rete pegs. The papillae are heavily infiltrated with histiocytes, a smaller number of polymorphonuclear leukocytes and edema. MacCallum-Goodpasture stains for bacteria are negative. The specific nature of the changes is not suggested, except that similar microscopic abscesses within the epidermis are seen in psoriasis."

The knee joints, the puncture of which yielded seropurulent fluid, never showed extreme swelling and redness, and they cleared up by the beginning of January 1945, although the patient complained of occasional aching.

Besides the bilateral seropurulent conjunctivitis, bilateral keratitis also developed on December 9 together with some superficial ulceration on the right cornea. He was treated with local and supportive measures and was given an occasional five day course of sulfadiazine. The latter seemed to have no effect on the disease.

The patient lost about 30 pounds (13.6 Kg.) within two months. The muscles around the knees wasted away severely. His mental condition was extremely poor, bordering on melancholia and lethargy. He was given 10 units of insulin twice daily from Jan. 15, 1945 until the date of his transfer to a general hospital on March 3. He also received four transfusions of 500 cc. of whole blood. From February 1 until March 3 he was given hot Sitz baths daily and two gentle prostatic massages weekly. About the middle of February his general condition improved and the cutaneous lesions also showed a remarkable improvement. At the time of his transfer to a general hospital on March 3, 1945 for further treatment and disposition, his condition was fair. He had gained weight, and the ocular, articular and cutaneous lesions had cleared up, with good motility of the joints and with slightly reddened and freely sweating areas on the hands and feet.

COMMENT AND SUMMARY

Keratosis blennorrhagica, often referred to as gonorrheal keratosis, while a rare disease, is perhaps not so rare as previously thought, as evidenced by the fact that we have been able to collect 166 case reports, including our own, in an exhaustive review of the medical literature. This number of cases exceeds by far the number previously reported.

This disease occurs predominantly in men in the fourth decade of life who have had repeated attacks of gonorrheal urethritis. The mortality of keratosis blennorrhagica is approximately 10 per cent.

The usual sequence of events is an initial chronic gonorrheal urethritis with local complications followed by gonorrheal arthritis. Soon

thereafter the characteristic symmetric lesions of the skin occur, showing a predilection for the extremities, the areas around the involved joints and the genital regions. Rarely the scalp and the mucous membranes of the mouth are involved. Bilateral conjunctivitis and other ocular complications occur frequently. A prolonged systemic reaction ensues, often ending in death.

We have analyzed in detail the numerous conflicting opinions concerning the cause of this grave and spectacular disease. The preponderance of evidence points definitely to a gonorrheal origin in the vast majority of cases, although in about a score of cases no evidence of gonorrheal infection whatsoever has been found.

As far as we can determine from a study of the literature, no author has ever estimated the percentage of cases of keratosis blennorrhagica in which gonococci were demonstrated in the cutaneous lesions. The fallacious belief that gonococci are practically never found in the cutaneous lesions may result from the fact that most authors were successful in collecting less than half a dozen case reports in which gonococci were found in the lesions of the skin. In striking contrast to this, we have found 17 reports of gonococci in the cutaneous lesions in 166 cases of keratosis blennorrhagica, an incidence of approximately 10 per cent. If to these figures are added the cases in which gonococci have been found in nonkeratotic gonorrheal lesions of the skin, then gonococci have been demonstrated in 12.2 per cent of the cases of all types of gonorrheal exanthemas. In contrast to this relatively high percentage, the blood on culture, it seems, only rarely yields gonococci. We have collected from the literature 5 reports of cases of typical keratosis in which gonococci were cultured from the blood and 18 reports of cases of nonkeratotic gonorrheal exanthemas in which the blood contained gonococci. Positive cultures from joints and eyes have been reported only occasionally.

Arthropathic psoriasis bears only a superficial resemblance to keratosis blennorrhagica. There are numerous differential diagnostic points.

In several recent reports Reiter's disease has been confused with keratosis blennorrhagica. In our opinion, a critical analysis of many of the cases in the literature reported as Reiter's disease does not exclude the probability of a gonorrheal infection.

We have reviewed at length the complex theories concerning the manner in which gonococci can produce such a violent and often fatal infection as is seen in keratosis blennorrhagica. The most logical explanation appears to be that, while a bacteremia of short duration develops, the protracted and grave picture of the disease is due to an extreme degree of bacterial allergy to the gonococci and their endotoxins.

We report a classic case of keratosis blennorrhagica in a 25 year old soldier in whom there developed, in order of sequence, chronic gonorrheal urethritis; bilateral conjunctivitis, keratitis and corneal ulcers; polyarticular arthritis; keratotic lesions of the skin, of the hard palate and of the soft palate, and balanitis circinata sicca.

In this dawn of penicillin therapy it is of great interest to note that the injection of over 5.000,000 Oxford units of penicillin neither prevented the development of the full-grown picture of keratosis blennorrhagica nor appreciably influenced its course.

RECURRENT GENITO-ORAL APHTHOSIS AND UVEITIS WITH HYPOPYON (BEHCET'S SYNDROME)

Report of Two Cases

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THIS is a report on cases of a recently (1937) described clinical entity of recurrent ulcerations of the oral cavity and genitals and of repeated attacks of uveitis which, in later stages, is associated with hypopyon. The disease of the eyes may lead to complete loss of vision.

Cases of this syndrome had already been reported before 1937. Blüthe [1] in 1908, Adamantiades [2] in 1931 and Dascalopoulos [3] in 1932 observed patients with this triad. In 1937, Behcet [4] gave the syndrome the name of triple symptom complex, when he recognized the interrelationship of various pathologic processes in one patient. More cases of the triple syndrome or of part of it will, in all probability, be found in the literature reported by dermatologists or gynecologists as cases of recurrent ulcus vulvae acutum or, erroneously, of chancroids, by internists and dentists as cases of recurrent oral aphthae and by ophthalmologists as cases of recurrent iritis, iridocyclitis or uveitis with hypopyon. Some of the accompanying manifestations may have been overlooked, since each specialist may have limited his field of observation.

From the Department of Dermatology, Columbia University, College of Physicians and Surgeons.

1. Blüthe, L.: Zur Kenntnis des recidivierenden Hypopyons, Inaug. Dissert., Heidelberg, D. Straus, 1908.

2. Adamantiades, B.: Sur un cas d'iritis à hypopyon récidivant, Ann. d'ocul. **168**:271-278, 1931.

3. Dascalopoulos, N.: Sur deux cas d'uvéite récidivante, Ann. d'ocul. **169**:387-393, 1932.

4. Behcet, H.: Ueber rezidivierende, aphthöse, durch ein Virus verursachte Geschwüre im Mund, am Auge und an den Genitalien, Dermat. Wchnschr. **105**:1152-1157, 1937; Considérations sur les lésions aphtheuses de la bouche et des parties génitales, aussi que sur les manifestations oculaires d'origine probablement parasitaire, et observations, concernant leur foyer d'infection, Bull. Soc. franç. de dermat. et syph. **45**:420, 1938; Kurze Mitteilung über Fokalsepsis mit aphthösen Erscheinungen am Mund, Genitalien und Veränderungen an den Augen als wahrscheinliche Folge einer durch Virus bedingten Allgemeininfektion, Dermat. Wchnschr. **107**:1037-1040, 1938; Some Observations on the Clinical Picture of the So-Called Triple Symptom Complex, Dermatologica **81**:73-83, 1940.

Most of the fully developed cases were observed in Europe (Behcet [4] in Istanbul, Turkey; Jensen [5] in Denmark; Franceschetti and Valerio,[6] Knapp,[7] Schultheiss-Linder [8] and Mach, Babel and Naville [9] in Switzerland; Whitwell [10] in England; Weekers and Reginster [11] in Belgium; Gilbert [12] in Germany; Weve [13] in the Netherlands, and Cavara [14] in Italy). Recently, two reports were published from Palestine; one from Jerusalem by Ephraim,[15] whose patient had ocular lesions of a questionable nature (trachoma?) and the other from Tel Aviv by Berlin,[16] whose patient had fatal complications of the central nervous system. Additional reports of cases of the complete syndrome have recently become

5. Jensen, T.: Sur les ulcérations aphtheuses de la muqueuse de la bouche et de la peau génitale combinées avec les symptomes oculaires (-Syndrome Behcet), Acta dermat.-venereol. **22**:64-79, 1941.

6. Franceschetti, A., and Valerio, M.: L'uveite récidivante (ad ipopion) manifestazione parziale di una sindrome muco-cutaneo-oculare, Rassegna ital. d'ottal. **9**:1-40, 1940.

7. Knapp, P.: Beitrag zur Symptomatologie und Therapie der rezidivierenden Hypopyoniritis und der begleitenden aphthösen Schleimhauterkrankung. Schweiz. med. Wchnschr. **71**:1288-1290, 1941; Zur Therapie der rezidivierenden Hypopyoniritis und ihrer Begleitkrankheiten, Ophthalmologica **103**:11-14, 1942.

8. Schultheiss-Linder, H.: Beitrag zur Symptomatologie und Therapie der die rezidivierende Hypopyoniritis begleitenden Genitalulcera und über die Beziehung derselben zum Ulcus vulvae acutum Lipschütz und zu den Vitaminen des B-Komplexes, Schweiz. med. Wchnschr. **71**:1290-1293, 1941.

9. Mach, R. S.; Babel, J., and Naville, M.: Syndromes muco-cutanés avec complications oculaires (érythème polymorphe, iritis récidivante aphteuse), Helvet. med. acta **7**:552-564, 1941.

10. Whitwell, G. P. B.: Recurrent Buccal and Vulval Ulcers with Associated Embolic Phenomena in the Skin and Eye, Brit. J. Dermat. **46**:414-419, 1934.

11. Weekers, L., and Reginster, H.: Contribution à l'étude de l'iritis récidivante à hypopion (uvéite allergique récidivante à hypopion), Bull. Soc. belge d'opht., 1938, no. 76, pp. 31-44; Un nouveau syndrome: Iritis, ulcères aigus de la bouche et de la vulve; sa parenté avec l'iritis récidivante à hypopion, Arch. d'opht. **2**:697-705, 1938.

12. Gilbert, W.: Zur Frage der Iridocyclitis mit rezidivierendem Hypopyon ("Iritis septica"), Klin. Monatsbl. f. Augenh. **71**:409-414, 1923.

13. Weve, H.: Ueber rezidivierende, allergische Staphylokokkenuveitis, Arch. f. Augenh. **93**:14-39, 1923.

14. Cavara, V.: Ueber ein besonderes Syndrom, gekennzeichnet durch rezidivierende Hypopyoniritis verbunden mit Geschwüren des Mundes und der Geschlechtsteile und mit Hautausschlägen, Klin. Monatsbl. f. Augenh. **104**:629-644, 1940.

15. Ephraim, H.: Triple Symptom Complex of Behcet: Report of a Case, Arch. Dermat. & Syph. **50**:37-38 (July) 1944.

16. Berlin, C.: Behcet's Syndrome with Involvement of Central Nervous System: Report of a Case with Necropsy, of Lesions of the Mouth, Genitalia and Eyes; Review of the Literature, Arch. Dermat. & Syph. **49**:227-233 (April) 1944.

available. Foss [16a] as well as Rygh [16b] described 2 cases in men, Bechgaard [16c] observed a young man who suffered from Behcet's syndrome preceded by ileitis and Jensen [16d] saw a case of Behcet's syndrome associated with ulcerative hemorrhagic colitis.

One of my patients exhibited the fully developed triple syndrome, while the other had lesions only in the mouth and on the vulva. Since it may take a long time (twenty-one years in Whitwell's [10] case 3) before the associated process becomes manifest and since all three signs will not in every case be present simultaneously in each patient, instances of genital and oral lesions alone are considered in this paper as belonging to this clinical entity. Cavara,[14] Franceschetti and Valerio [6] and Berlin [16] also considered cases in which these two signs were shown as being typical cases of the syndrome. There are far too many cases on record of simultaneous or successive occurrence of genital and oral aphthae to consider the existence of the two differently located conditions as coincidental. In some reports the genital and oral lesions were recurrent (Popoff [17]; Cole and Driver [18]; Whitwell,[10] cases 2 and 3; Walter and Roman [19]; Michaelis [20]; Grütz [21]; O'Leary [22]; Gray [23]; Wien and

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16a. Foss, B.: Die doppelseitige rezidivierende Hypopyon-uveitis, Behcet's Syndrome, Acta ophth. **19**:293-329, pts. 3-4, 1941.

16b. Rygh, H.: Aftose stomatitter med stesiedt hendlikke paa Behcet syndrom, Tidsskr. f. d. norsk. laegefor., 1941, no. 10, p. 453.

16c. Bechgaard, P.: Case of Recurrent Aphthous Stomatitis Accompanied by Conjunctivitis and Ulcerations of Genitals and Skin, Ugesk. f. læger **102**:1019-1023 (Oct. 3) 1940.

16d. Jensen, J. S.: Ulcerous Hemorrhagic Colitis Associated with Behcet Syndrome, Ugesk. f. læger **106**:176 (Feb. 24) 1944.

17. Popoff, L.: L'ulcère vulvaire aigu de Lipschuetz comme manifestation particulière de l'érythème polymorphe et d'érythème noueuse, Bull Soc. franç. de dermat. et syph. **45**:1254-1268, 1938.

18. Cole, H. N., and Driver, J. R.: Ulcus Vulvae Acutum with Oral Lesions (Periadenitis Mucosa Necrotica Recurrens), Arch. Dermat. & Syph. **32**:119 (July) 1935.

19. Walter, F., and Roman, I.: Beitrag zur Kenntnis der hämatogenen Hautmetastasen bei Ulcus vulvae acutum, Dermat. Wchnschr. **90**:705-709, 1930.

20. Michaelis, O.: Ulcères et aphtes récidivants de la bouche et de la vulve, Bruxelles-méd. **17**:336-341, 1937.

21. Grütz: Stomatitis et vulvitis aphthosa chronica recidivans (blastomycetica?), Zentralbl. f. Haut- u. Geschlechtskr. **20**:415-416, 1926.

22. O'Leary, P., in discussion on Becker, S. W.: Aphthae; Acne Rosacea; Involvement of the Scrotum and Thigh, Arch. Dermat. & Syph. **28**:254 (Aug.) 1933.

23. Gray, A. M. H.: Case of Ulcerative Stomatitis? Nature, Proc. Roy. Soc. Med. (Sect. Dermat.) **17**:57, 1924.

Perlstein [24]; Kumer,[25] case 2; Jaffé [26]; Fordyce [27]; Berlin,[16] case 2; Schugt [28]; Carol and Ruys [29]; Ebert and Wolff [30]; Matras [31] and Gibson [32]), while in others a single instance of coexistence of the two manifestations was reported (Planner and Remenovsky [33]; Pils [34]; Talalov [35]; Carol and Ruys,[29] case 3; Sarazin [36]; Kumer,[25] case 1, and Chauffard, Brodin and Wolf [37]). The prognosis for patients with genital and oral lesions becomes more serious if one considers the possibility of ocular and other complications.

The fact that in various instances other combinations of the triad occur—e. g., ocular and genital (Blobner [38]) or ocular and oral lesions (Franceschetti and Valerio,[6] case 3; and Cavara,[14] case 2, and Dascalopoulos,[3] case 2)—is further proof that these three signs are manifestations of one disease. It would be going too far to consider as abortive forms of the syndrome cases with only one recurrent mani-

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24. Wien, M. S., and Perlstein, M. O.: Ulcus Vulvae Acutum Associated with Lesions of the Mouth, J. A. M. A. **98**:461-466 (Feb. 6) 1932.

25. Kumer, L.: Ueber Haut- und Mundschleimhauterscheinungen beim Ulcus vulvae acutum, Dermat. Ztschr. **57**:401-411, 1930; Zur Frage des Ulcus vulvae acutum, Zentralbl. f. Haut- u. Geschlechtskr. **31**:417, 1929; Arch. f. Dermat. u. Syph. **160**:97-98, 1930.

26. Jaffé, K.: Ulcus vulvae acutum mit aphthenähnlichem Ulkus an Zunge, Dermat. Wchnschr. **90**:691, 1930.

27. Fordyce, J. A., in discussion on Fox, H.: Aphthous Stomatitis of Twenty-Three Years' Duration, Arch. Dermat. & Syph. **2**:256-257 (Aug.) 1920.

28. Schugt, P.: Ulcus vulvae acutum (Lipschütz) und seine Ätiologie, Ztschr. f. Gynäk. **49**:2180-2185, 1925.

29. Carol, W. L. L., and Ruys, A. C.: On Aphthosis and Ulcus Vulvae Acutum, Acta dermat.-venereol. **9**:123-141, 1928; Over aphthosis en ulcus vulvae acutum, Nederl. tijdschr. v. geneesk. **1**:396-406, 1928.

30. Ebert, M. H., and Wolff, M. J.: Vulvitis (Ulcerative) and Stomatitis, Arch. Dermat. & Syph. **30**:472-473 (Sept.) 1934.

31. Matras, A.: Ueber aphthenartige Mundschleimhautveränderungen beim Ulcus vulvae acutum mit positivem Bacillus crassus Befund, Arch. f. Dermat. u. Syph. **166**:491-497, 1932.

32. Gibson: Case of Recurrent Buccal and Vulvar Ulcers, Brit. J. Dermat. **50**:664-665, 1938.

33. Planner, H., and Remenovsky, F.: Beiträge zur Kenntnis der Ulcerationen am äussern weiblichen Genitale, Arch. f. Dermat. u. Syph. **140**:162-188, 1922.

34. Pils, H.: Ein Beitrag zur Aphthosis, Arch. f. Dermat. u. Syph. **149**:4-8, 1925.

35. Talalov, J. Z.: Ulcus Vulvae Acutum Accompanied by Disease of Skin and of Oral Mucosa, Arch. Dermat. & Syph. **30**:510-516 (Oct.) 1934.

36. Sarazin, cited by Brocq, L.: Traité élémentaire de dermatologie pratique, Thesis, Paris, Doin, 1907, vol. 1, p. 869.

37. Chauffard, A.; Brodin, P., and Wolf, M.: Stomatite et vulvite aphtheuses, suivies de troubles démentiels passagers, Bull. et mém. Soc. méd. d. hôp. de Paris **47**:841-844, 1923.

38. Blobner, F.: Zur recidivierenden Hypopyoniritis, Ztschr. f. Augenh. **91**:129-139, 1937.

festation, such as repeated attacks of severe oral aphthae. The ultimate course of the disease in these patients, or more knowledge of the cause of the syndrome, however, may show that their cases also belong to the entity under discussion.

REPORT OF CASES

CASE 1.—J. T.,[39] a single man of Italian parentage, born in the United States was first seen in the Eye Institute[40] in 1941, at the age of 21. He gave a history of urethral discharge some years previously, with swelling of the testicles. He repeatedly had sores on the genitals and sores of the gums and lips and had "kernels" in both inguinal areas in 1936. He admitted frequent intercourse with prostitutes. In January 1939 the left eye became inflamed, and one week later the right eye also became inflamed. An operation (pansinusectomy) was undertaken, and for a short time improvement of the condition of the eyes was noted. Cultures from the antrum yielded a type XXIX pneumococcus. Attacks of severe pain in both eyes recurred fairly frequently, however, and in 1941 hypopyon of the left eye was observed for the first time. Iridectomy of both eyes in July 1941 and cyclodiathermy of the left eye in September 1941 did not stop the ocular process. A diagnosis of uveitis with hypopyon was made. Cultures of material from the left conjunctiva yielded Staphylococcus aureus.

In September 1941, the vitreous of the right eye was cloudy, and there was a large area of choroiditis in the macular area. Down and temporally, there were white bands of proliferation of retinal tissue. The left eye showed dense opacity of the lens. The fundus was not seen, and no reflex was obtained. There were many floaters in the vitreous. Treatment with atropine, sulfadiazine, sulfathiazole and injections of typhoid vaccine may have had some effect on the hypopyon present, but attacks of pain with hypopyon recurred about every three to four weeks. In October 1941, the left eye was enucleated. Attacks of hypopyon of the right eye continued. In March 1942, the vision of the right eye was 15/200.

The main features of the pathologic report were the following: There was striking infiltration of the iris by polymorphonuclear leukocytes. The ciliary body, the lower portion of the choroid, the retina and the optic nerve were infiltrated by lymphocytes. The retina was completely detached, and there was detachment of the choroid and of the posterior portion of the ciliary body. There was an exudate extending from the surface of the ciliary body, below and beyond along the interior surface of the iris and across the interior lens capsule to join a lesser band of exudate from the upper ciliary processes. The choroid above showed only a slight cellular infiltration in its interior portion. The episcleral vessels over the lower portion of the globe were surrounded by inflammatory cells.

While in the Eye Institute, the patient had several attacks of pain in both ankles and shoulders. In September 1941, swelling of the right ankle with some puffiness was noted. A roentgenogram disclosed osteoarthritis of a mild degree. In January 1942, the patient suffered from myositis or fibrositis of the back.

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39. This patient was presented twice at the New York Academy of Medicine, Section of Dermatology and Syphilis: at the October 1943 meeting; (Arch. Dermat. & Syph. **50**:137 [Aug.] 1944) with the diagnosis of left postoperative anophthalmos, uveitis and choroiditis of the right eye, possibly due to the virus of lymphogranuloma venereum and again at the October 1944 meeting, with the diagnosis of Behcet's triple symptom complex. (ibid. **53**:147 [Feb.] 1946)

40. Dr. Maynard Wheeler gave me permission to report this case.

In 1941 multiple abscesses of the axillas developed; in 1942 the patient had a low grade chronic sinusitis and the sinuses were irrigated. In May 1942, superficial small ulcerations of the gums were noted. On Aug. 28, 1942, genital ulcerations of three weeks' duration were discovered.

Physical examination disclosed a healthy-looking young man. His temperature was normal. He had a scar on the left side of the lower lip. He suffered from mild acne of the face and back and a pyogenic infection of the right big toe. On each side of the scrotum he had a dime-sized crateriform ulceration (fig. 1) with no

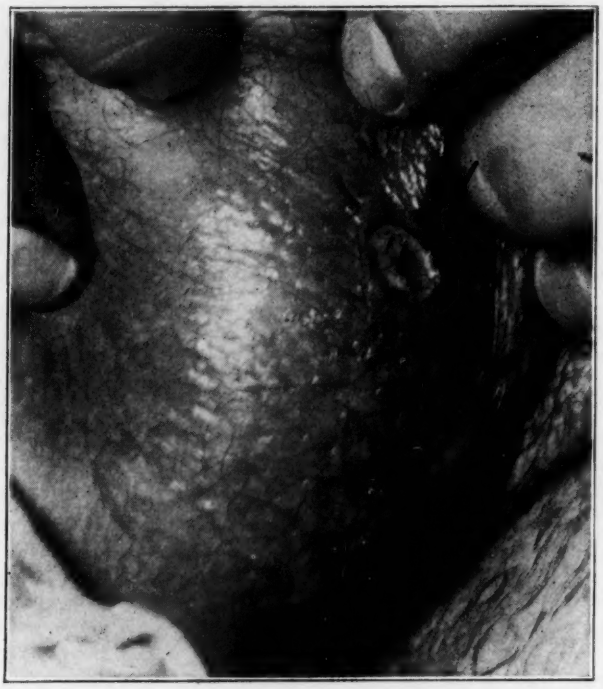

Fig. 1 (case 1).—Ulceration on left side of scrotum.

induration of the periphery and with a dirty, purulent base. The inguinal lymph nodes were not enlarged. Three dark field examinations as well as smears for Ducrey's bacillus (Bacillus ulceris mollis) and Bacillus crassus were negative. Frei and Ducrey tests repeatedly elicited strongly positive reactions. A control test with isotonic solution of sodium chloride produced mild redness. Reactions to the Wassermann and Kline tests were negative on several occasions. Further physical and roentgenologic examination showed that the lungs were normal. Tests with tuberculin in dilutions of 1:100,000 and 1:10,000 elicited negative reactions; in a dilution of 1:1,000 the reaction was positive. The spleen was palpable. The prostate gland was slightly enlarged. No gonococci were found in the prostatic smear. Dental roentgenograms showed no foci. The urine gave negative reactions for albumin and glucose. The white blood cell count ranged between 10,000 and 16,000. The differential white cell count did not show any abnormalities. The serum proteins were 7.4 Gm. (albumin 5.3 Gm. and globulin 2.1 Gm.) per hundred cubic centimeters. The rectal examination showed

normal conditions. Since at that time it was thought that the ophthalmic process was possibly due to the virus of lymphogranuloma venereum, therapy with Frei antigen intravenously and with sulfathiazole orally was instituted. No chill or fever followed the first injection. The vitreous cleared considerably, and a large choroidal lesion was visible. On October 27, while the patient was still under treatment with sulfathiazole and Frei antigen, hypopyon again developed.

When the patient was seen in August 1944, no more attacks of iritis had occurred but only light perception of the right eye was present. He had suffered from recurrent attacks of small lesions in the mouth and showed several aphthous ulcers of the buccal mucosa. He also had several attacks of large genital sores, and when seen in August and September 1944, he had large dirty-looking ulcerations on the right side of the scrotum without inguinal adenitis. He was admitted to the Eye Institute for a course of injections of penicillin amounting to 2,400,000 units. The genital lesions practically healed within four days; his vision improved slightly. While he was under treatment with penicillin, a large boil developed on his back and there was inflammation at the site of some injections of penicillin on the buttocks. The temperature at that time rose to 101 F. Frei and Ducrey tests were repeated and reactions were again strongly positive. The reaction to a control test with isotonic solution of sodium chloride was negative. When the patient was last seen, on Nov. 7, 1944, no new genital or oral lesions had occurred during the preceding five weeks. The condition of the eye had remained unchanged.

CASE 2.—E. O'C.,[41] aged 21, a single woman born in New York city of Irish and French-Canadian parentage, has been under observation since 1942. She is next to the youngest of nine children, three of whom died early in childhood. No other member of the family has a similar disease. She has suffered from recurrent mouth lesions since childhood. Menstruation started when she was 14. At the age of 13, she noticed the first vulvar lesions. They have since recurred often. At the beginning they appeared between the menses; lately they have sometimes coincided with the menses. Some attacks begin with chills. Temperatures around 101 F. may persist for a few days. The ulcerations heal with deep scars, leading to destruction of the vulva. At the beginning of the attack a mucous discharge is discernible. Sometimes the inguinal glands of the side involved are inflamed. In former years, attacks were accompanied by severe pains in the left or the right calf. Lately the attacks of oral ulcerations have been extremely severe and so frequent that the patient has not been free from them at all. The patient says that she has not had sexual relations. She has always been in good general health. She has never been absent from New York city for any length of time.

Examination.—The physical examination revealed essentially normal conditions. Psychiatric studies ruled out the possibility that the lesions were self inflicted. A roentgenogram showed that the lungs were normal. There was no enlargement of the lymph nodes. The eyes were normal. The tonsils were small and could hardly be considered foci of infection. Examination of the teeth (November 1944) showed that the upper right central incisor and the lower right cuspid were abscessed. They were removed.

Mouth: The inner surfaces of the lips, the tonsils, the tongue, the soft palate and the hard palate (and rarely the buccal mucosa) were the sites of superficial or deep tender ulcerations which were covered with an exudate and surrounded by a red halo (fig. 2). The ulcerations had a deep, dirty base. Scars of healed lesions were seen on the tongue, lower lip and soft palate.

41. This patient was presented at the New York Academy of Medicine, Section of Dermatology and Syphilis, on March 6, 1945, with a diagnosis of Behcet's syndrome, abortive form (?).

Genitals (fig. 3): The vulva was the site of an extensive indurative, atrophic and destructive process. Both labia majora were extensively scarred. The posterior part of each labium majus was removed by plastic operation (1942), and biopsy studies of the tissue were made. Both labia minora were enlarged and showed multiple fenestration. When the ulceration began, the central portion was necrotic with a surrounding hemorrhagic border. Deep ulcerations often measured 5 cm. in diameter. The base of such a large ulceration was granulating, and the border was infiltrated.

The uterus was slightly retroverted and the small adnexa were not felt. On one occasion, the cervix was found to be normal and on another to show an erosion.

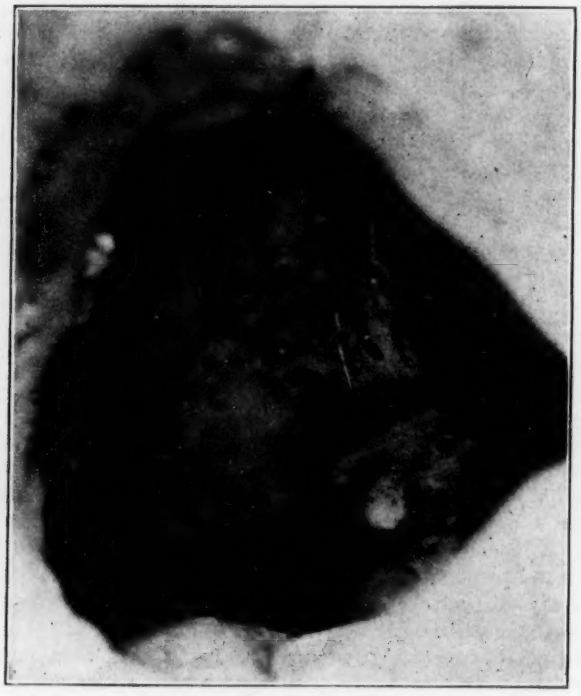

Fig. 2 (case 2).—Confluent aphthous lesions of the soft palate.

Laboratory Examination.—The urine did not contain albumin or glucose. Repeated Wassermann and Kline tests elicited negative reactions. The number of white cells ranged between 11,850 and 15,900. The blood count showed 92 per cent hemoglobin, 4,850,000 red cells and a differential count of 72 per cent polymorphonuclear leukocytes, 22 per cent small and 5 per cent large lymphocytes and 1 per cent mononuclear leukocytes. The sedimentation rate was 35 to 40 mm. per hour. Cultures of blood (during the patient's stay in the hospital) and of material from the throat and the nose showed no growth. Blood agglutination tests with Bacillus typhosus O and H and with B. paratyphosus A, B and C gave negative results. Reactions to Frei and Ducrey tests were repeatedly negative. Tests with old tuberculin in a dilution of 1:10,000 produced negative reactions.

Bacteriologic Studies: Genital lesions. Results of dark field examinations and of examinations of scrapings for Donovan bodies and of smears for chancroid

bacilli and for inclusion bodies were all negative. Slides and cultures failed to demonstrate fungi, and autoinoculation tests gave repeatedly negative results. Smears of material from the cervix and the ulceration were negative for gonococci. B. crassus was once seen in great numbers in a smear from the genital lesion; it was not found in the biopsy specimen. In a culture of material from the lesions, Staph. aureus and Staph. albus but no anaerobes were found.

Oral lesions: On smears inclusion bodies and B. crassus were not seen. In a culture Staph. aureus, Staph. albus and streptococci were found.

Virus Studies[42]: Suspensions in isotonic solution of sodium chloride were made from genital and oral scrapings. The suspensions were inoculated into mice, guinea pigs, cotton rats, embryonated hen's eggs and chick embryo tissue cultures of the Li-Rivers type. There was no evidence of the growth of any virus.

Fig. 3 (case 2).—Vulva showing ulceration (*A*) of left labium majus, fenestration (*B*) of left labium minus, fibrous bands (*C*) and extensive scarring. The posterior part of each labium majus was removed by plastic operation.

Biopsy (labium majus, specimen obtained at plastic operation): The granulation tissue at the base of the ulceration was swollen and edematous (fig. 4). Areas below the ulceration were the sites of a chronic inflammatory reaction with aggregation of polymorphonuclear leukocytes, lymphocytes and plasma cells. The infiltration was not found in any significant distribution around the blood vessels, which appeared thickened. Giemsa stains did not reveal the presence of any organisms. The histopathologic diagnosis was genital ulceration of unknown cause.

Course and Treatment.—In May 1942, a plastic operation of the vulva was performed in the Sloane Hospital for Women. For a while the patient had no recurrence of the genital lesions. About one year later, the ulcers began to recur

42. The virus studies were made by Miss E. Molloy.

fairly often (every three or four weeks). She was successively treated locally with 3 per cent sulfathiazole ointment, potassium permanganate soaks and estrogen cream (genitals) and with a solution of hydrogen peroxide, throat lozenges containing nupercaine, and estrogen cream (mouth). The patient avoided brushing her teeth for several weeks and eliminated chicken, eggs and oatmeal from her diet.

General treatment consisted of injections of liver extract, the ingestion of nicotinic acid (100 mg. twice daily) and sulfathiazole (2 grains [0.13 Gm.] daily

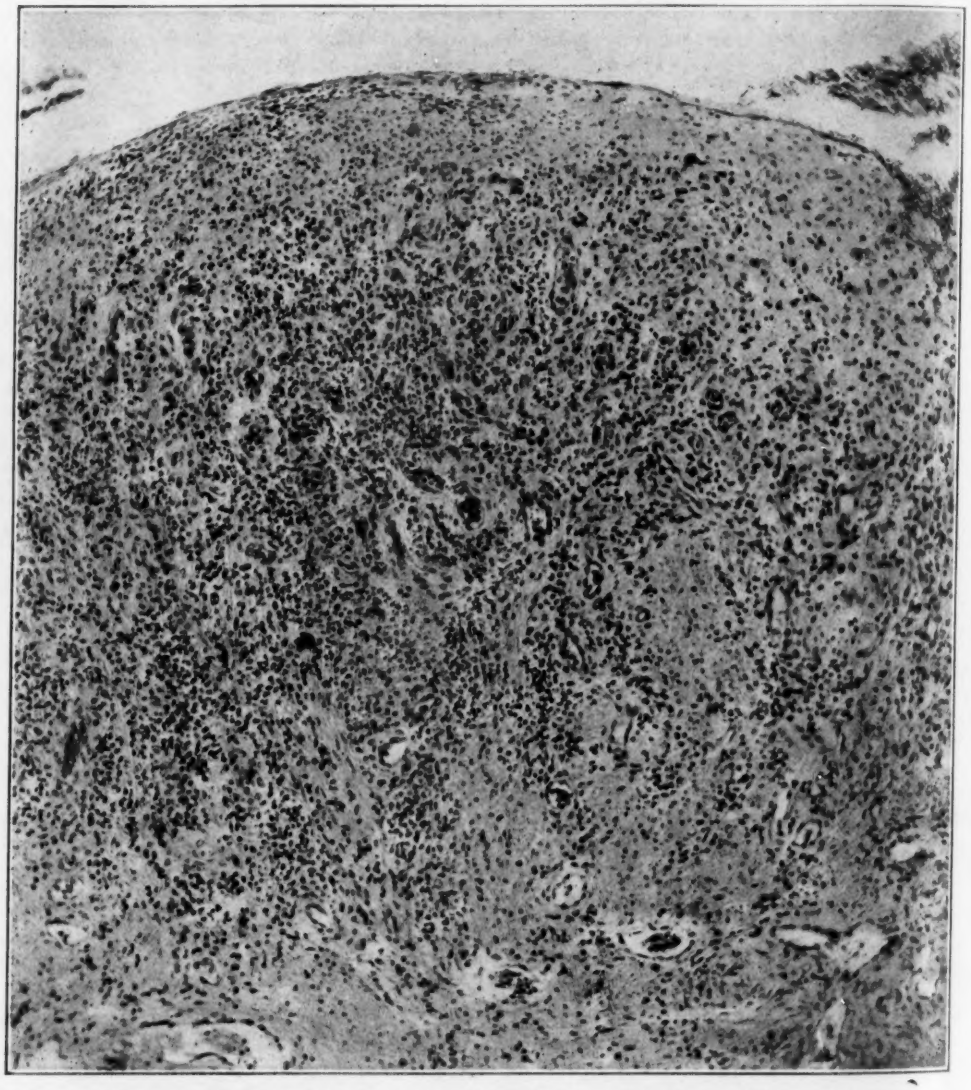

Fig. 4 (case 2).—Photomicrograph of ulceration of left labium majus, showing chronic inflammatory reaction below ulceration. The specimen was obtained at a plastic operation.

for six days), injections of penicillin (1,710,000 units, given at the Presbyterian Hospital), the removal of two abscessed teeth and vaccination for smallpox. Each of these therapeutic attempts was given up when the impression was gained that it made the disease worse rather than better. Under treatment with penicillin especially, the extent of the patient's oral lesions became greater than ever. After the vaccination the patient had no oral lesions for two weeks. There was then a recurrence in the form of deep ulcerations of the uvula and tonsils. The genital lesion which had already been present at the time of the vaccination failed to heal and presented a large 3 by 7 cm. deep necrotic ulceration six weeks after the vaccination. With the application of penicillin ointment the lesion slowly became cleaner. Recently, the patient married and became pregnant. She consulted me again in her fourth month of pregnancy. Attacks of oral and genital lesions had become so frequent that several ulcerations in different stages were seen in the oral cavity and on the vulva. Tyrothrycin ointment and others, one of 40 per cent cod liver oil with 1 per cent zinc borosalicylate (Vitaguent) and the second of a bacterial antigen in a base of anhydrous wool fat with zinc oxide, ammonium sulfoichthyolate and sodium borate (Antipeol), were applied locally to the vulval lesions, which subsequently became cleaner. New ulcerations, however, continued to appear. The oral cavity was treated with compound solution of sodium borate. She complained of pain in the lower part of the thighs. Delivery by cesarean section is planned.

COMMENT

Eyes.—Involvement of the eye constitutes the gravest manifestation of the triad. It may be the first, second or third and last sign of the disease. The course of the disease of the eyes in the man (case 1) was similar to that observed in other patients. For a while only one eye is involved; later the other eye invariably shows the same changes. In a few instances the disease has started in the two eyes simultaneously. The attacks occur every three to four weeks, or about that frequently. They are characterized by intense periorbital pain and photophobia. The pericorneal reaction is usually mild; there are precipitations in Descemet's membrane. Iritis or iridocyclitis develops later. Either the anterior part of the eye, with or without involvement of the retina and choroid, shows the first pathologic changes, or the posterior parts of the eye manifest retinochoroiditis or periphlebitis (Blobner [38]). In both instances hypopyon is a late symptom. All authors have noted that the hypopyon tends to disappear rapidly (in two to three days), while the vitreous clears slowly and sometimes incompletely. After every attack the vision remaining is definitely diminished. The impairment of the vision progresses to complete blindness in both eyes. Loss of vision is attributed either to posterior synechias with occlusion of the pupil and (secondary) atrophy of the optic nerve (Mach, Babel and Naville,[9] Adamantiades [2]), to secondary glaucoma (Cavara [14]) or to lack of transparency of the vitreous, which cannot recover during the short intervals between the frequent attacks (Franceschetti and Valerio [6]).

Enucleation of one eye, which was undertaken in my patient (case 1) and in patients reported on by Kawabata,[43] Blüthe,[1] Blobner,[38] Weve,[13] Adamantiades[2] and von Hippel,[44] has no influence on the disastrous course of the disease in the other eye.

The enucleated bulbus shows infiltration of both the iris and the ciliary body with polymorphonuclear leukocytes and of the choroid with lymphocytes. In most of the bulbi a thick membrane extends through the bulbus, pulling the retina forward (Weve,[13] Blobner[38] and Kawabata[43]). This membrane was missing in von Hippel's,[44] Nakayama's[45] and my patient. The retina is usually found detached, degenerated and infiltrated, and large hemorrhages are seen in front of and behind it. The optic nerve is infiltrated and more or less atrophic. There was no evidence of tuberculosis in any of the histologic specimens, and whatever stains for bacteria were made failed to show organisms (von Hippel[44] and Blüthe[1]). The pathologic observations suggested to von Hippel[44] that the ocular disease was caused by a metastatic pustular process, transmitted through the central vessels of the retina and the long ciliary arteries.

Erythema Nodosum.—My 2 patients never suffered from erythema nodosum, which occurred in many of the reported cases whether the patients had two or three of the classic symptoms (Jensen[5]; Whitwell,[10] case 2; Weekers and Reginster[11]; Knapp[7]; Koeppe[46]; Sicharulidze[47]; Adamantiades[2]; Blobner[38]; Katznelson[48]; Reis[49]; Pils[34]; Ephraim[15]; Planner and Remenovsky[33]; Franceschetti and Valerio[6]; Chauffard,

43. Kawabata: Ueber den histologischen Befund einer Iridocyclitis recidivans mit Hypopyon, Chuo-Ganka-Iho **27**:29-32, 1935; abstracted, Zentralbl. f. d. ges. Ophth. **35**:209, 1936.

44. von Hippel, E.: Ein Fall von Iridocyclitis mit recidivierendem Hypopyon mit anatomischem Befund, Arch. f. Ophth. **128**:272-279, 1932.

45. Nakayama, N.: Beitrag zur Kenntnis der pathologischen Anatomie der sogenannten recidivierenden Hypopyonuveitis, Arch. f. Ophth. **116**:249-263, 1925. In his case only one eye was diseased! Oral and genital manifestations were missing.

46. Koeppe, L.: Klinische Beobachtungen mit der Nernstspaltlampe und dem Hornhautmikroskop: Ein Fall von doppelseitigem, recidivierenden Hypopyon, kombiniert mit Opticusatrophie, im Bilde der Nernstspaltlampe, Arch. f. Ophth. **94**:267-270, 1917.

47. Sicharulidze, I.: Zur Frage der recidivierenden Hypopyoniritis im Zusammenhang mit Erythema nodosum, Arkh. oftal. **8**:658-663, 1932; abstracted, Zentralbl. f. d. ges. Ophth. **28**:566, 1933.

48. Katznelson, A.: Recidivierende Hypopyon-iritis und Erythema nodosum, Russk. oftal. zurn. **4**:484, 1925; abstracted, Zentralbl. f. d. ges. Ophth. **16**:127, 1926.

49. Reis, W.: Augenerkrankungen und Erythema nodosum, Klin. Monatsbl. f. Augenh. **44**:203-224, 1906.

Brodin and Wolf [37]; Popoff [17]; Samek and Fischer [50]; Scherber [51]; Mach, Babel and Naville [9]; Dreyer,[52] and Pautrier, Ullmo and Baumeister [53]). Cutaneous eruption was described by Bussalai,[54] Talalov [35] and Michaelis [20] as erythema polymorphe. Grütz [21] observed on the extremities doughy infiltrations which discharged a thin, bloody exudate. In this case blastomycetes was seen in the tissue.

Rheumatic Pain.—Gollwitzer's [55] patient and my female patient complained of drawing pains in the legs whenever a genital sore developed, but there was no redness of the skin. Jensen's [5] patient had pains in the forearms. My male patient suffered from recurrent attacks of arthritis of the ankles and of fibrositis of the back. The patients of Adamantiades,[2] Blobner,[38] Weve,[13] Matras,[31] Popoff [17] (case 1), and Ephraim [15] had more or less severe arthritis; Whitwell's [10] patient (case 1) had acute edema of the leg.

Cutaneous Infections.—Various cutaneous infections are described as associated with the syndrome: boils (Reis,[49] Gilbert,[12] Cavara [14]), pustules of the forehead (Jensen [5]), pyoderma (Mach, Babel and Naville,[9] Franceschetti and Valerio [6]) and sycotic and seborrheic eczema (Cavara [14]). My male patient had acne of the face, recurrent boils, multiple abscesses of the axilla and at one time some infection of the right big toe. The female patient was free of cutaneous infections.

Positive Reactions to Skin Tests.—It is interesting to note in connection with these frequent cutaneous infections that some authors find a decided nonspecific hypersensitivity of the skin. At least at certain times all intradermal tests may result in a reaction which, in some cases, is indistinguishable from a positive reaction to the test. This reactivity was considered to be based on pathergy (Urbach), which does not

50. Samek, J., and Fischer, E.: Erythema nodosum als bakterielle? Metastase eines Ulcus vulvae acutum, Arch. f. Dermat. u. Syph. **158**:729-733, 1929.

51. Scherber, G.: Klinik und Bakteriologie der pseudotuberkulösen Geschwüre sive Ulcus vulvae acutum: Nachweis der Identität der in den Geschwüren sich findenden Bazillen mit den Scheidenbazillen Döderleins und auf Grund dieser Festellung Vorschlag, die Geschwürsform Scheidenbazillengeschwüre zu benennen, Arch. f. Dermat. u. Syph. **127**:359-391, 1919; in discussion on Pautrier, Ullmo and Baumeister.[53]

52. Dreyer, in discussion on Pautrier, Ullmo and Baumeister.[53]

53. Pautrier, L. M.; Ullmo, A., and Baumeister, M. P.: Erythème noueux et ulcère aigu de la vulve de Lipschütz, Bull. Soc. franç. de dermat. et syph. **45**:1221-1226, 1938; L'erythème noueux aux cours de diverses infections, ibid. **45**:1207-1213, 1938.

54. Bussalai: Ulcus vulvae acutum di Lipschütz, Soc. ital. di dermat. e sif., Boll. d. sez. ital. **2**:134, 1934.

55. Gollwitzer, M.: Ueber rezidivierende Hypopyon-Iritis mit Ausgang in doppelseitige Erblindung, Inaug. Dissert., Würzburg, Ochsenfurt, Fritz & Rappert, 1938.

constitute an antigen-antibody reaction. Even a prick with a sterile needle results in a pustule (Jensen [5]), and on the skin of the genitals the resulting pustule may go on to necrosis. Blobner,[38] Ephraim,[15] Foss [16a] and Jensen [5] elicited reactions to all sorts of intradermal tests and controls with isotonic solutions of sodium chloride. The positive reactions of my male patient to the Frei and Ducrey tests had been considered, on previous occasions when Behcet's syndrome was still unknown to me, as some proof for the diagnosis of chancroid of the genitals and uveitis due to lymphogranuloma venereum. At present, in the light of reports on Behcet's syndrome, this diagnosis seems highly improbable. At no time were chancroid bacilli found in the ulcerations. A picture of recurrent large genital ulcerations which do not possess an undermined border, which as a rule do not cause involvement of the inguinal glands and in which demonstration of the Ducrey bacillus is impossible is not typical of chancroids. If the positive Frei and Ducrey reactions in this case were specific they would refer to some infection with chancroid bacilli and the virus of lymphogranuloma venereum in the past. The patient once had a bubo, and he admitted frequent intercourse with prostitutes. If the positive reactions were nonspecific, it would be hard to explain why results of other tests—for instance, tuberculin in high dilutions and control tests—were negative. (On one occasion an injection of isotonic solution of sodium chloride elicited some redness.) The female patient showed no reactions to repeated tests with Ducrey vaccine and Frei antigen. Apparently, unspecific reactions to various skin tests are not encountered in all cases of the disease. Their occurrence may be seen only in patients with a history of, or in the presence of, spontaneous pustular infections of the skin.

Genital Ulcerations.—The genital ulcerations were much more destructive in the woman (case 2) than in the man (case 1). They sometimes started with general symptoms (chills and high fever). In the beginning they consisted of large grayish necrotic areas. When the slough disappeared large, well demarcated defects of tissue were visible, which either healed with extensive scarring or, if they occurred on the thin parts of the small labia, with fenestration. For many years the lesions appeared between the menses; later they developed with the menses. Reports in the literature do not permit any conclusions as to the role of menstruation. In the man the occurrence of genital lesions was not accompanied by systemic signs and did not incapacitate the patient. Pain and accompanying symptoms were negligible. The inguinal lymph nodes of the man did not swell; those of the woman did so occasionally.

Histology.—Histologically, the genital ulceration of the young woman did not show any characteristic changes, owing perhaps to the chronic stage of ulceration in which the biopsy was performed. Popoff [17]

found epithelioid cells with lymphocytes, histiocytes, plasmocytes and mast cells as well as with occasional giant cells. Perivascular round cell infiltration, which Berlin [16] saw in cerebral, ocular and genital lesions of his patient, was not observed in the genital lesion of my female patient. However, infiltration of the episcleral vessels of the man was noted. Kawabata [43] saw perivasculitis of the retina.

Oral Lesions.—The oral lesions were much more fully developed in the female patient. Since childhood she had rarely been free from them. They occurred on the lips, tonsils, tongue, soft and hard palate and only rarely on the buccal mucosa. The base of the ulcers was covered with a grayish exudate, and the margin was usually surrounded by a red halo. They varied from the size of a pinhead to that of a millet seed and were extremely tender. The man only occasionally had tiny white lesions on his gums and his lower lip. Some of the oral lesions left scars. Jensen's [5] patient had twelve oral lesions at one time. While under treatment with penicillin the young woman exhibited confluent large aphthae involving almost the entire soft palate.

General Condition.—Usually the victims of the disease are young people, between 15 and 45 years of age. They appear to be in good health. Sometimes attacks of recurrent ulcerations start with chills and fever (as in the case of the woman when a genital lesion developed and in Gilbert's [12] patient when a hypopyon formed). Carol and Ruys [29] and Michaelis [20] noticed that three days before an attack the patient's liver became hard and enlarged, and they therefore ascribed the disease to some disturbance of the liver. In Knapp's [7] patient multiple sclerosis was also observed. Autopsy of Berlin's [16] patient, who died after a severe cerebral attack, revealed edema of the liver, small multiple foci of inflammation and softening of the brain.

Bacteriologic Observations.—B. crassus was found only in the genital lesions of women. The organism could not be recovered from oral lesions of the same woman or, as a rule, from oral and genital lesions in men. These genital ulcerations associated with oral aphthae do not differ from ulcus vulvae acutum as it was originally described by Lipschütz.[56] This author had already noted among his patients one in whom oral lesions also were present. His opinion that this occurrence was coincidental was not upheld by other observers, who remarked that a combination of recurrent genital and oral lesions seemed to be the rule. Numerous authors reported that B. crassus was found in many of the genital lesions. The bacillus was never, with the exception of Matras' [31] case, found in oral lesions. Matras also saw positive

56. Lipschütz, B.: Ulcus vulvae acutum (Lipschütz), in Jadassohn, J.: Handbuch der Haut- und Geschlechtskrankheiten, Berlin, Julius Springer, 1927, vol. 21, p. 392.

blood cultures and recovered B. crassus from cultures of material from the genital lesions. His results were somewhat similar to Samek and Fischer's [50] observation in a case of ulcus vulvae acutum without oral lesions; they were able to demonstrate B. crassus in the accompanying erythema nodosum (in cultures and histologic slides). These authors also obtained positive cultures of blood. I and all other observers, among them Wien and Perlstein,[24] Walter and Roman,[19] Cole and Driver,[18] Carol and Ruys,[29] Schugt [28] and Jaffé,[26] were able to demonstrate B. crassus in the genital lesions but were unable to observe the organisms in the oral lesions. It should be noted that B. crassus was also present in the urethral and vaginal secretions of Samek and Fischer's [50] patient, and it can be found in the same location in healthy persons where there is no sign of an ulcer. Positive results were never obtained when human beings were inoculated with cultures of B. crassus or with pus from the lesions. It was pointed out by Wien and Perlstein [24] that other factors besides B. crassus are apparently necessary for the formation of the ulcer. Either B. crassus is only a secondary invader or autoinfection with B. crassus, which ordinarily plays the role of a saprophyte, takes place (Lipschütz [56]). In the female patient B. crassus was once found abundantly in the genital lesion. In subsequent slides it was not seen; it was not found in the oral lesions or in the blood culture, and it was absent from the biopsy material of the genital ulcer. If, in addition, one considers that similar cases of genital and oral ulcers have been observed in men patients, in whom naturally B. crassus is absent, the role of this bacillus as an etiologic factor is of more than doubtful significance.

Behcet [4] found inclusion bodies in smears of material from ulcerations of the skin and the mucous membrane and considered that these observations were proof that he was dealing with a virus disease. Jensen,[5] Franceschetti and Valerio [6] and I could not confirm his results. In one of my patients, virus studies gave negative results. Franceschetti and Valerio [6] expressed a belief that a virus may use the intestinal tract as the portal of entry, since Carrère [57] observed good results from the energetic disinfection of the gastrointestinal tract. Cultures of material from the oral lesions sometimes yield Corynebacterium pseudodiphtheriticum (Jensen [5] and my female patient).

Cultures of Blood.—In some cases positive results from cultures of blood were obtained: (Cavara,[14] mildly pathogenic Staph. albus, and Adamantiades,[2] staphylococcus). Weve [18] referring to the accompanying articular process and erythema nodosum, stated that he considered the disease a manifestation of an allergic state against the staphylococcus. Foss,[16a] who is of the same opinion, regularly saw the onset of the eye

57. Carrère, L.: Iridocyclite purulente récidivante, Bull. et mém. Soc. franç. d'opht. **44**:345-352, 1931.

disease occurring two to three days after injections with staphylococcus toxoid vaccine. Weekers and Reginster [11] were uncertain as to the nature of the agent which causes the allergic reaction. The site of the manifestation develops greater sensitivity with every attack. Gilbert [12] explained the process in the eye as a metastasis and expressed a belief that the patient suffers from some form of sepsis lenta. Cavara [14] stated his opinion that a virus makes the body more susceptible to infections with the staphylococcus.

Etiology.—Behcet [4] expressed the firm belief that the disease is caused and maintained by a focus of infection. In his patients, treatment of diseased teeth lessened the frequency of attacks. This experience was not shared by many observers who searched for and removed all possible foci. Extraction of diseased teeth did not help in the cases of von Hippel [44] and Michaelis [20] and in the case of my female patient. Pansinusectomy in my male patient in 1937, tonsillotomy and tonsillectomy in Urbanek's [58] case and operation on a maxillary empyema in Weve's [13] patient did not halt the general trend of the disease.

It is only natural that tuberculosis as an etiologic factor in this chronic disease was widely discussed. More or less pronounced signs of tuberculosis were observed in the patients whose cases were reported by: Weekers and Reginster [11] (case 1, suspicious apexes), Jensen [5] (hemoptysis), and Dascalopoulos [3] (case 1, hemoptysis; case 2, opacities of the left apex). Some features of Staehli's [59] case of iritis (involvement of one eye only, absence of genital and oral lesions) in a man with generalized tuberculosis make it doubtful that this was a case of Behcet's syndrome. In spite of lack of convincing evidence Gilbert,[12] Kawabata,[43] Ito,[60a] Shigeta [60b] and Nakayama [45] expressed their belief in the tuberculous nature of the disease. Urbanek [58] regarded the manifestations as allergic signs of tuberculosis. Pillat,[61] who observed chronic dysentery in his tuberculous patient, expressed the opinion that a mixed infection with tubercle bacilli and other organisms explains the disease, since formation of hypopyon coincided with attacks of dysentery. Touraine [62] regards Behcet's syndrome as a grave manifestation of "aphthosis." This term covers various diseases with aphthous lesions, which appear in recurrent attacks and are located on the mucous membrane.

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58. Urbanek, J.: Fall von beiderseitiger recidivierender Hypopyonuveitis, Ztschr. f. Augenh. **83**:357-364, 1934.

59. Staehli, J.: Zur Frage der endogenen recidivierenden Hypopyon-Iritis, Klin. Monatsbl. f. Augenh. **34**:721-731, 1922.

60. (*a*) Ito: Nippon Gankwa Gakukwai Zasshi **25**:1082, 1921; cited by Nakayama [45]; (*b*) Shigeta: ibid. **28**:516, 1924; cited by Nakayama.[45]

61. Pillat, A., in discussion on Urbanek.[58]

62. Touraine, A.: L'aphtose, Presse méd. **46-47**:571-573, 1941.

Therapy.—Before the era of the sulfonamide drugs and penicillin, general hygienic measures and local treatment of the ocular, genital and oral lesions were tried. The attacks subsided, but the lesions recurred. In the case of the man, the futility of local measures for the eye is clearly demonstrated. Following the suggestion of Knapp [7] and of Weekers and Reginster,[11] sulfathiazole was given to him, with the result that there were no more attacks of hypopyon, but there was continued recurrence of the oral and genital lesions. Sulfanilamide was given orally without effect in Knapp's,[7] and in Franceschetti and Valerio's [6] case. Sulfathiazole did not influence the oral and genital lesions in my case 2. Transfusions, which were of no avail in Cavara's [14] case, proved helpful to Blobner's [38] patient. Following Knapp's [7] suggestion, the woman (case 2) was treated with vitamin B (liver and nicotinic acid); her condition, however, became decidedly worse. While receiving treatment with injections of penicillin she had the severest outbreak of oral lesions ever observed in her. Five weeks after the completion of penicillin treatment the male patient had had no recurrence of oral and genital lesions and the ocular process was quiescent. After the woman was vaccinated with smallpox vaccine she was free from oral lesions for two weeks, but the genital lesions showed at the same time decided exacerbation.

SUMMARY

A review of the literature reveals that instances of the fully developed syndrome (recurrent iritis or uveitis with hypopyon and recurrent genital and oral ulcerations) had been observed prior to Behcet's description of the syndrome. The first American case of this disease is described. The patient was a young man with typical lesions of the eye which had led to the enucleation of one eye and to blindness of the other, with recurrent genital ulcerations and with mild recurrent oral aphthae. The case of a young woman with recurrent genital and oral aphthous lesions is also reported. Her case is included in the cases of the syndrome, since the oral and genital manifestations in this case are identical with those seen in cases of Behcet's [4] syndrome. It may take many years before another manifestation of the triad develops. In this case the genital ulceration of the young woman is identical with the lesion described as ulcus vulvae acutum by Lipschütz.[56] Bacteriologic studies yielded no clue to the causative factors, and the trial of various therapeutic measures (including the administration of vitamins, the removal of foci, vaccination, the ingestion of sulfonamide compounds and the injection of penicillin) gave no satisfactory results.

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ACUTE LUPUS ERYTHEMATOSUS DISSEMINATUS TREATED WITH PENICILLIN

Report of a Case

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ALTHOUGH the etiologic agent of lupus erythematosus disseminatus is still a matter of controversy, there are some investigators who believe that there is sufficient evidence at the present time to justify the opinion that this disease is caused by streptococci or their products. Streptococci have been isolated from the blood in a number of cases of the disseminated type and O'Leary,[1] among others, is of the opinion that those micro-organisms are of etiologic importance.

If this opinion is correct, it stands to reason that the administration of penicillin should be beneficial to a patient with lupus erythematosus disseminatus. It might be well to recall at this point that similar reasoning was employed when the sulfonamide compounds were first introduced into therapy, and although encouraging results following the oral administration of these compounds have been reported the results in general were disappointing.[2]

Having tried the various known methods of treatment in a case of subacute lupus erythematosus, including the recently advocated internal administration of iodine,[3] and having failed miserably, I decided to give the patient penicillin. The result was so gratifying that the case is here reported.

REPORT OF CASE

R. E. D., a 46 year old white man, was referred to me in March 1945 for the treatment of an eruption involving the hands, arms, neck, chest, back and legs, which was of seven months' duration. The patient's past, personal and family histories were irrelevant.

Present Illness.—In July 1944 the patient had a severe sunburn, following which he noted a slight itching sensation on the chest and arms, but no eruption

1. O'Leary, P. A., in discussion on Belote, G. H., and Ratner, H. S. V.: The So-Called Libman-Sacks Syndrome, Arch. Dermat. & Syph. **33**:642 (April) 1936.

2. Strakosch, E. A., in Spink, W. W.: Sulfonamides and Related Compounds in General Practice, ed. 2, Chicago, The Year Book Publishers, Inc., 1942, chap. 12.

3. Cannon, A. B.: Treatment of Lupus Erythematosus Disseminatus by Internal Administration of Iodine, Arch. Dermat. & Syph. **51**:26 (Jan.) 1945.

was visible at that time. The first eruption noted by the patient appeared in September, when he observed "red papules" on the hands, arms and neck. His physician then told him that he might have psoriasis, but no treatment was given because the patient had to move to Denver. In February 1945 the eruption started to spread to the chest, back and legs.

Examination.—Examination showed a well developed and well nourished white man, apparently not seriously ill. The general physical examination (Dr. R. W. Vines) revealed normal conditions, with the exception of a cervical lymphadenopathy. On the dorsa of both hands and on the arms, neck, chest, back and thighs was a maculopapular eruption. The majority of the lesions resembled the iris lesions seen in erythema multiforme. Scaling was seen only in a few lesions.

Laboratory Data.—Examination of the blood performed on March 30, 1945 showed a hemoglobin content of 90 per cent, 4,680,000 red blood cells and 8,100 white blood cells per cubic millimeter, of which 78 per cent were polymorphonuclear neutrophils and 22 per cent lymphocytes. The sedimentation rate was 27 mm. (Westergreen) at the end of the first hour. The Wassermann reaction was negative. The urine and the blood chemistry were normal. A biopsy was performed, and the histologic section revealed edema in the cutis, extravasation of leukocytes and dilatation of the vessels in the papillary bodies.

Treatment and Further Course.—A tentative diagnosis of erythema multiforme was made, and because the patient complained of pains in the joints he was given sodium salicylate, 3 Gm. daily, and a mild antipruritic paste. He was next seen on April 6, at which time the lesions were spreading to the ankles and he complained of general malaise. The lesions were drier, and the scaling was increased; it was at that time that the diagnosis of subacute lupus erythematosus disseminatus was considered. He was then told to live on a high caloric and high vitamin diet and was given 3 Gm. of sulfadiazine daily and an iodine-containing ointment. Because the cervical lymph nodes were getting larger, he was referred to an otolaryngologist (Dr. G. L. Pattee) who found that both tonsils were infected and advised tonsillectomy, which was performed on April 9. After the operation the lesions faded considerably, and for the first time no new lesions appeared. Because the patient suffered a severe generalized reaction to the sulfonamide compound, the drug was discontinued and he was given iodine internally as recommended by A. B. Cannon.[3] After two days of iodine medication a severe itching of the entire skin developed, and the patient started to vomit several times. The iodine was then discontinued, and liver extract was given intramuscularly and vitamin B complex by mouth. By the end of April he had new lesions involving the face (butterfly distribution) and the forehead up to the hair line. He was then caught in a snowstorm and was exposed to the wind and cold for several hours. Subsequently he had chills and a fever, the temperature rising to 104 F., and numerous new erythematous lesions appeared all over the body. The diagnosis of acute lupus erythematosus disseminatus was made, and he was hospitalized for treatment with penicillin. At this time the hemoglobin content was 88 per cent, and he had 5,250 white blood cells per cubic millimeter. He was given 20,000 Oxford units of sodium penicillin intramuscularly every four hours around the clock. After five days of penicillin medication the itching of the skin disappeared, and all the lesions started to undergo involution. A total of 2,000,000 units of penicillin was given over a period of sixteen and a half days. He was then discharged from the hospital, feeling well and with the greater part of the lesions gone, although there was

still slight scaling left on the skin on his hands and neck. He was again seen one month after his discharge from the hospital, at which time the sedimentation rate and the results of all other laboratory studies were normal. At the time of writing his skin shows only depigmentation and hyperpigmentation over most of the parts formerly affected.

COMMENT

The rapid improvement of the patient suffering from acute lupus erythematosus disseminatus while receiving injections of penicillin may substantiate the theory that this disease is of streptococcic origin. It is realized that the good result obtained in this single case is not conclusive and that further observations with penicillin in the therapy of this disease are necessary before its value can be established.

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A DEVICE OF VALUE FOR ROENTGEN RAY EPILATION

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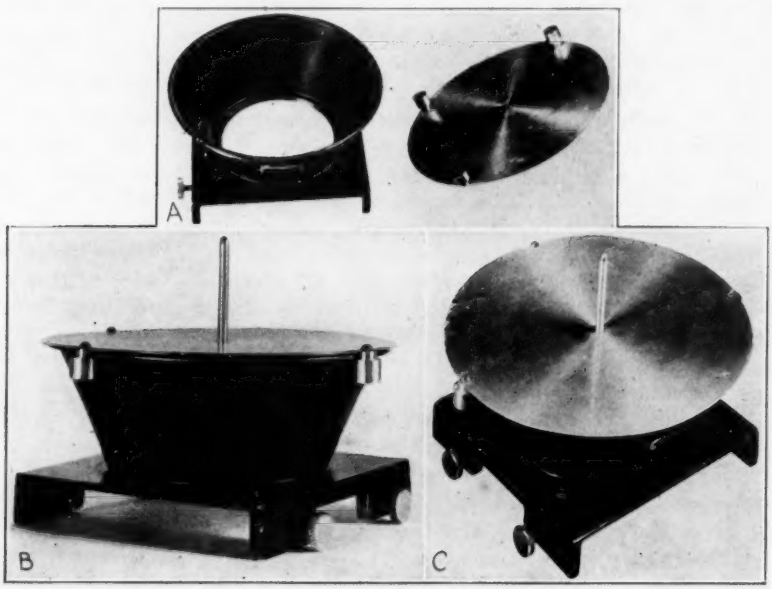
THE PERFORMANCE of roentgen ray epilation for tinea capitis is a technic requiring experience and skill on the part of the dermatologist. Formerly this treatment consumed several hours of time to insure its accurate performance. However, with the addition of various



Device for roentgen ray epilation. *A*. under surface of device and the x-ray cone to which it is attached before the treatment. *B*, side view of attached cone and device. *C*, view from above.

time-saving methods over a period of years, the procedure can now be carried out in less than one hour. Any method which may lessen the technical difficulties or lead to greater accuracy of performance is deemed worthy of report.

For several years, a device has been successfully employed in the dermatologic radiotherapy clinic of Mount Sinai Hospital. It had been

From the Dermatologic Radiotherapy Clinic of Mount Sinai Hospital. New York.

made in response to a request for some method which would lead to more accurate focusing of the roentgen rays on the five points of the Kienböck-Adamson fields. Prior to this, intersecting silk threads had been placed over the cone in a not particularly satisfactory effort to find the center. With the present method, a wide cone with a focus-skin distance of 15 cm. is placed over the portal of an x-ray tube. The device is so constructed as to slide (illustration) over this cone. It consists of a thin circular metal sheet of the same size as the cone. At the edges of this metal sheet are three small metal knobs, which permit the device to slide on and off the cone with ease. In the exact center of this metal sheet is a blunt steel rod which extends downward for an additional 5 cm., thus increasing the focus-skin distance to 20 cm. The roentgen ray technic, accordingly, incorporates a focus-skin distance of 20 cm. among its other physical factors.

In the actual performance of the epilation, the child is placed in the proper position and shielded with lead rubber. The device is placed on the cone. The flat surface of the device is then made parallel to the plane of the area of scalp under treatment, with the projecting rod touching the respective Kienböck-Adamson points. The x-ray tube is then locked into position and the device gently removed from the cone. This procedure is repeated for each of the five fields.

Other methods of improved fixation or centering of either the patient or the tube are in use, but this device has proved satisfactory during the performance of hundreds of roentgen ray epilations. For this reason, we are describing its use, with the expectation that other dermatologists may find it of value.

2 East Sixty-Ninth Street.

Clinical Notes

LYMPHANGIOMA CIRCUMSCRIPTUM

Successful Results of Treatment with Solid Carbon Dioxide

JAMES Q. GANT JR., M.D., SURGEON (R),
United States Public Health Service
BETHESDA, MD.

Lymphangioma circumscriptum was first described in 1879 by Tilbury Fox and Colcott Fox, under the title of "Lymphangiectodes,"[1] although Tilbury Fox had given a suggestive description of this disease entity in 1862.[2] The name "lymphangioma circumscriptum" was given to the disease by Morris in 1893,[3] and it seems to be an appropriate one, even though many synonyms appear in the literature. Various forms of therapy have been advocated, varying from roentgen rays to cauterization. Because of the scarring which would result, I decided to use solid carbon dioxide.

REPORT OF A CASE

C. G., a white woman aged 26, reported that vesicular lesions of the skin developed in the right subscapular area when she was 6 months old. Since that time this area has never been entirely free of the eruption. However, the number of the lesions varied from time to time. Mild trauma resulted first in a clear vesicle which finally became filled with blood. After several days the bloody vesicle fluid was absorbed, and the vesicle again became clear. If a vesicle is ruptured, it continues to ooze for several minutes to half an hour or even longer. The clear vesicular lesions appeared to arise spontaneously, apparently without trauma, on normal skin; they might remain for many weeks, and then they were gradually absorbed. Trauma usually resulted in new vesicle formation.

Routine physical examinations revealed no abnormalities, and results of laboratory tests were within normal limits.

Dermatologic Examination.—There was a 14 by 20 cm. patch of irregularly grouped yellowish and red visicles and papulovesicles on the right subscapular area. The subcutaneous tissues were unaffected. The vesicles varied from 1 to 8 mm. in diameter; some were transparent to yellow, while others were red to purple. Their walls were thickened and were not easily ruptured. When a yellowish vesicle was intentionally ruptured, a clear fluid escaped; this flow

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From Dermatoses Section, Industrial Hygiene Division, Bureau of State Services.

1. Fox, T., and Fox, T. C.: On a Case of Lymphangiectodes, Tr. Path. Soc. London **30**:470, 1879.

2. Pusey, W. A.: The History of Dermatology, Springfield, Ill., Charles C Thomas, Publisher, 1933, p. 126.

3. Morris, M.: Lymphangioma Circumscriptum, in Unna, P. G., and others: Internationaler Atlas von seltener Hautkrankheiten, Leipzig, L. Voss, 1889.

continued for several minutes to half an hour and was in excess to the amount of fluid contained in the vesicle. This fluid was alkaline in reaction to Fisher alkacid tester paper (the test color was yellow-green, indicating a p_H of 7 to 8). There was some telangiectasia at the base of the clear vesicles (fig. 1, *A*).

The skin between the vesicles appeared normal with no scarring at sites of previous lesions.

Histopathologic Examination.—The area below the epidermis showed large spaces whose walls consisted of a single layer of endothelial cells, apparently lymph spaces. The epidermis immediately above the lymph spaces showed absence

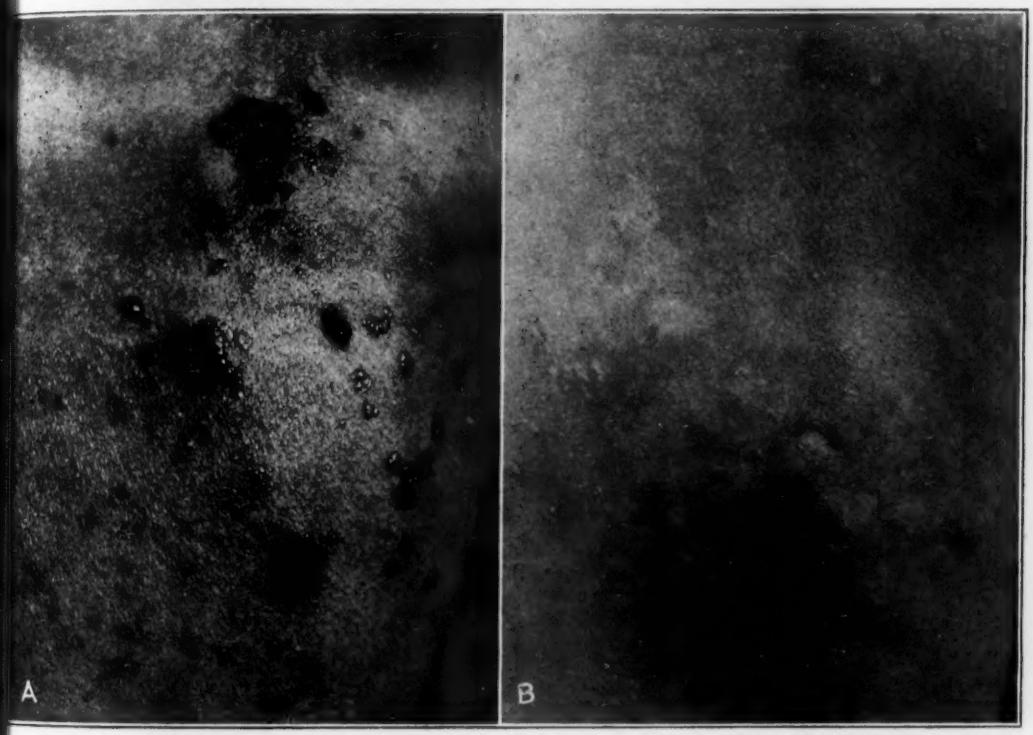

Fig. 1.—*A*, vesicular, hemorrhagic lesions below right scapular area; *B*, appearance of skin ten months after treatment.

of papillary bodies but otherwise appeared normal. Below the lymph spaces there was a scattered diffuse infiltration with lymphocytes and dilated capillaries. There was also an increase in the fibroblasts and fixed tissue cells (fig. 2).

Clinical Course.—Individual lesions were treated with solid carbon dioxide cut into pencils of irregular shapes. The pencils were so shaped and applied that irregular scarring was produced; thereby the production of a series of regular scars, which would be more noticeable, was avoided. Moderately firm pressure was maintained on individual lesions for forty to sixty seconds.

Treatment was carried out over four months. This was necessary since it was impossible to predict the areas that were pathologic until vesicles developed. Occasionally a lesion had to be treated more than once, but none required more than two treatments.

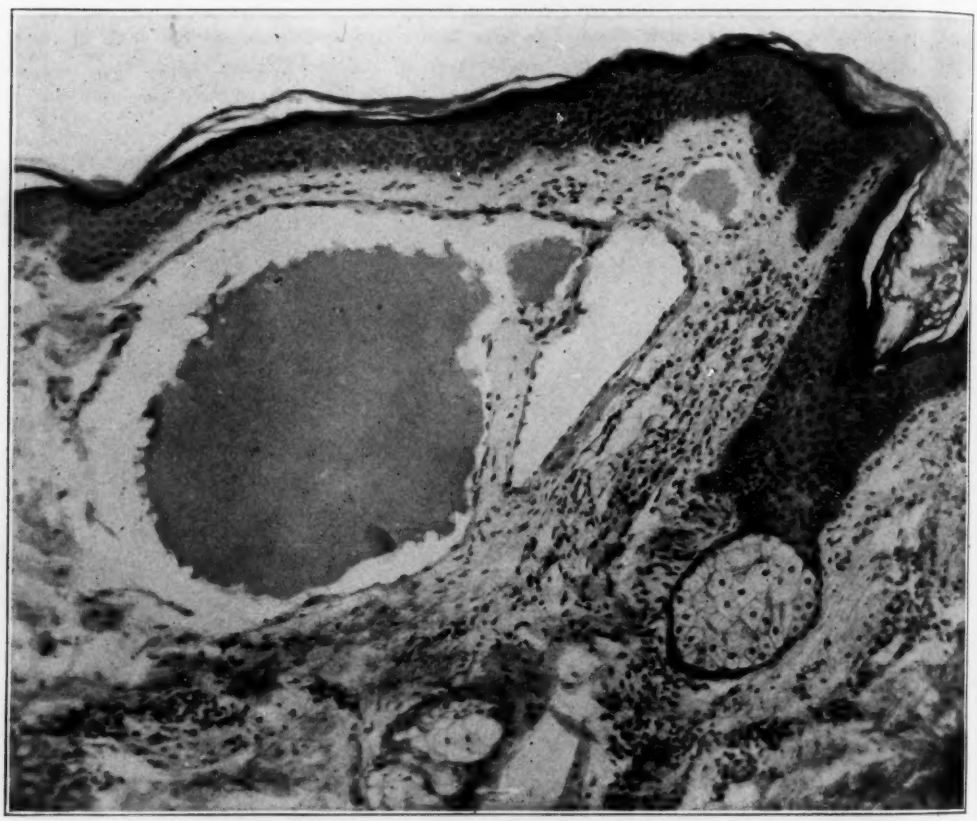

Fig. 2.—Photomicrograph showing spaces directly below the epidermis. Hematoxylin and eosin; × 73.

Immediately after the freezing, the vesicle became hemorrhagic. This was followed in a few days by crust formation, and in approximately thirty days there remained only a faint white scar (fig. 2).

There has been no recurrence of lesions over a period of ten months.

SUMMARY

The case of a 26 year old woman with lymphangioma circumscriptum which had been present since she was 6 months of age is reported. An excellent cosmetic and therapeutic result was obtained with the use of solid carbon dioxide.

1726 M Street, Northwest Washington 6, D. C.

A YAWS CLINIC IN NEW GEORGIA

LIEUTENANT COMMANDER LAUREN SOMPAYRAC (MC)
and
LIEUTENANT COMMANDER HARRY SPENCE (MC)
United States Naval Reserve

We were on duty at the United States Naval Hospital at Munda, New Georgia. In the spring and summer of 1944 we noticed symptoms of yaws on the skins of the natives. As we were indebted to these friendly people for the solicitous help they gave our armed forces, we felt that we might in some measure repay them by establishing a clinic for the treatment of yaws. The higher echelon permitted us to begin such a clinic at Wana Wana, a native village about an hour and a half by power boat from Munda.

Accordingly, we secured a thatched hut in the sprawling, fly-infested village. Though we were working under primitive conditions, we attempted to work scientifically; yet owing to the exigencies of war, our records were lost; only an incomplete graph and some pictures remain. Therefore this can in no sense be considered a scientific paper; rather, it is a setting down of facts remembered because they were so sharply etched in our minds.

Every patient was given a physical examination and a Kahn test. Notes on therapy and progress were taken. We held a total of thirteen weekly clinics, during which we saw more than 300 patients. A reliable laboratory reported that over 95 per cent of these natives had positive serologic reactions. It is interesting that no primary lesions were seen on the genitals. This observation confirmed our belief that yaws is not passed on by sexual intercourse, contrary to a natural suspicion arising from the fact that yaws resembles syphilis. With one exception, a lesion on the buttocks of an infant, all primary lesions were on the faces of children. These primary lesions were fleshy without much induration. Secondary lesions were likewise observed in young people, were maculopustular and were distributed like those of a secondary syphiloderm. We noted that the commonest secondary lesion was observed on the feet of young children, in the form of multiple ulcers. These frequently resulted in a manifestation called "crab yaws," a name originating in the peculiar waddling gait of patients with these painful sores.

We noted bony deformities of the forearm and the condition called "saber shin." Pain in the joints was reported by patients with these symptoms, and it was of interest that in later stages of yaws, especially among the older people, the only symptom of the disease was pain. No changes were observed in the central nervous system or in the heart.

The uncleanliness of the natives was a positive factor contributing to the prevalence of the disease, for we found that the clinically well natives were the physically clean natives. The native women, uncomfortably adjusting themselves to European customs, reported to our clinic considerably burdened by dirty layer after dirty layer of pieces of cloth which they had fashioned into a covering supposed to resemble a dress. Visiting them at their homes, we found that they had discarded this covering for the more comfortable groin

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This article has been released for publication by the Division of Publications of the Bureau of Medicine and Surgery of the United States Navy. The opinions and views set forth in this article are those of the writers and are not to be construed as reflecting the policies of the Navy Department.

wrap-around (*lava-lava*). In spite of the difficult conditions under which we labored, we had many medical volunteers for this clinic. Both corpsmen and medical officers were required to wear rubber gloves; although the disease is contagious, fortunately none of the white personnel contracted it.

All ih all, our results were good. We used bismuth preparations and oxophenarsine hydrochloride in dosages recommended by the International Conference on Syphilis. All lesions subsided after four injections, with the exception of some ulcers on the ankle which were resistant to the therapy. We found that a minimum of eight weekly injections were required for a clinical clearing. The serologic reaction was not reversed in a single instance, even after observations based on a total of thirteen weeks of the recommended treatment.

No matter how hazardous our mission may have seemed to us at first, we found the natives eager to take our treatment. As a matter of fact, our own initial skepticism about their ultimate intentions led us to secure from the British Commissioner both a native Samoan doctor and a guard. One might be tempted to say that the natives in some instances were too eager to take what they called the "needle treatment." On one occasion a young woman was told to bend her arm to hold the alcohol sponge; she returned to her home and came back to us a week later with the arm tightly bound in a sling and with the sponge, now filthy, still on the cubital fossa.

We held our clinic at Wana Wana from about 9 a. m. to 3 p. m., one day each week. Our patients came from the nearby villages on foot and from the adjoining islands in quaintly colorful dugout sailing canoes. They cooperated with us in every way possible. If our sterilizer was blown out, they would organize a singing group, lustily singing the native version of "Onward Christian Soldiers." After our eighth clinic, the head man of the village had his villagers bring us great quantities of fruit, mats, shells, beads, native fishhooks, walking canes and baskets.

That the natives took to us kindly is well illustrated by their daily greeting, "Muna muna Lana," which is their way of saying, "Good morning!" Some magic, almost mystic, messenger service seemed to apprise the natives of our arrival at the clinic; for after our ride over in the boat, loaned to us by the Army for this purpose, we would find the natives lined up, ready for treatment and happily smiling.

DERMATITIS DUE TO PREPARATION AND ADMINISTRATION OF PENICILLIN SOLUTION

HERMAN GOODMAN, M.D., NEW YORK

Reports of dermatitis from penicillin among physicians are unusual. Pyle and Rattner gave a short summary of the case of a medical officer.[1] One hears of eruptions among workers in factories making and packaging the preparation.

REPORT OF A CASE

M. D., a physician aged 50, a native-born American, had administered penicillin for eighteen months with no damage or irritation. On June 15, 1945 he noticed itching, redness, tiny vesicles and oozing in an area ¼ inch (0.6 cm.)

1. Pyle, H. D., and Rattner, H.: Contact Dermatitis from Penicillin, J. A. M. A. **125**:903 (July 29) 1944.

square on the outer side of the middle finger of the right hand. This area corresponded to the site of pressure of the syringe when administering the solution of penicillin. The area involved by the dermatitis increased peripherally until it covered the surface of the outer side of this finger. On June 20 he noticed a similar area on the outer side of the middle finger of the left hand. This corresponded to the site of pressure when the syringe was carried immediately prior to and after administration. Several precautions were taken. The skin was covered with a protective cream and a layer of powder was placed over the cream. Surgical gloves were worn. These gloves were removed in the conventional manner. The wrist of one glove was grasped by the fingers of the other hand; sometimes the left was removed first, and other times the right was removed first. New areas of dermatitis appeared on the inner surfaces of the wrists where contact was made by the fingers of the gloved hands while removing the gloves.

By July 15 these areas were involved: on the right hand, the middle phalanx of the middle finger, the middle joint of the third finger and the inner surface of the wrist; on the left hand, the middle joint of the index finger, the outer surface of the middle finger, the middle phalanx of the third finger and the inner surface of the wrist. Tiny vesicles and itching were noticed at the site of pressure of the bow of the eyeglasses on the left ear. This area corresponded to the section of bow utilized to lift the glasses from the eyes. The left upper lid and the skin of the left infraorbital area became itchy; tiny vesicles appeared, and the skin became darker than normal. Blurring of the sight of the left eye was noticed, and it persisted.

The areas of affected skin were covered with a mixture of bentonite and talc through the vesicular phases. Unfiltered fractional doses of roentgen rays were administered and relieved the itching. All contact with penicillin was stopped. Fresh vesicles ceased to appear, and the oozing stopped. The areas of skin involved in the acute response to the insult with penicillin became denuded and the subkeratin layers scaled. The borders of the lesions on the fingers presented overhanging fringes of keratin. These were cut.

Conventional patch tests with solutions of trademarked sodium penicillin elicited positive reactions. The site of contact was extremely pruritic.

On August 23 the left periorbital area was darker than the right and the sight was slightly blurred. The areas of skin of the fingers were scaly and rough. The wrists showed a slight lichenification with itching, particularly on pressure.

COMMENT

The skin of a physician reacted by the appearance of dermatitis venenata after contact with small amounts of solution of conventional penicillin marketed as sodium penicillin. The physician had never previously reacted to any chemical or combination of chemicals. The p_H of the solution of commercial penicillin may have been one factor in the production of the dermatitis venenata. The infinitesimal amount of solution of penicillin transferred from the gloved left hand to the skin of the ear caused the appearance of vesicles and intense itching. The solution of sodium penicillin must, then, be a member of the rare group of materials exciting a dermatitis in smallest amount or in lowest concentration in a few persons. Physicians, pharmacists, technicians and others engaged in preparing the contents of vials of sodium penicillin for solution or topical application must consider any irritation of the skin as dermatitis venenata due to penicillin. Precautions should be taken to stop contact on the first appearance of the eruption.

Warning to the patient making topical application of penicillin is also necessary; he should stop the application if the area becomes irritated.

NOTE.—June 5, 1946: It was learned that the visual fields had been contracted. The physician had become color blind, being unable to distinguish the special color charts in any combination. Despite the avoidance of direct or indirect contact with penicillin, the sites of the original eruptive lesions, middle fingers and third fingers, continue to exhibit dermatitis, itching and slight oozing on exposure to many other things formerly utilized without reaction. On exposure to natural sunlight for half an hour, on May 25, 1946, each of the orbital regions became red, swollen and itchy and continued in diminishing degree until this date. Dark prescription glasses had been worn but afforded no protection.

SPOROTRICHOSIS

Report of a Case of Its Occurrence in California

A. GELBER, M.D., LOS ANGELES

E. H., a white man aged 51, an amateur horticulturist, was first seen on June 2, 1942, when he gave a history of having scratched his left index finger six weeks before while working in his garden. He considered the injury trivial until a hard "pimple" developed at the site of injury and began to ulcerate. Prior to referral he had used topical applications which consisted mainly of compresses of magnesium sulfate and zinc oxide ointment.

Examination revealed a well nourished man whose only abnormality was a bluish red punched-out ulcerated area discharging a serous exudate on the dorsal aspect of his left index finger. There was no ascending lymphangitis on the forearm and no involvement of epitrochlear or axillary nodes. A tentative diagnosis of sporotrichosis was made. Cultures of material taken from the ulcer were made on Sabouraud's medium. Syphilitic gumma was ruled out by failure to observe spirochetes on dark field examination and by negative Wassermann and Kline reactions. Tuberculosis was eliminated by the negative reaction to tuberculin in high dilution and by a roentgen ray examination of the chest and pyoderma by a normal blood sugar level. Coccidioidomycosis was ruled out by direct smears, culture and animal inoculation. Repeated efforts to find the organism on direct smears were unsuccessful. The culture which grew readily at room temperature on Sabouraud's medium yielded Sporotrichum schencki on the seventh day. Microscopically the mycelium appeared as hyaline, fine branching organisms 1 to 2 microns in diameter. The spores were oval to pear shaped and were attached to short lateral branches or longer hyphae, showing rosette configuration. A cutaneous test with sporotrichin antigen 1:10 and a complement fixation test elicited strongly positive reactions. A suspension of the Sporotrichum culture was injected intraperitoneally into a male white rat, in which severe orchitis and peritonitis developed. Smears of pus from lesions in testes revealed numerous gram-positive cigar-shaped organisms.

Administration of saturated solution of potassium iodide was instituted within the first few days. A patch test with potassium iodide elicited a negative reaction. The patient had a swelling of the submaxillary node and rhinitis when the 45 minim (2.8 cc.) level was reached. Because of his intolerance to potassium iodide he was given roentgen ray therapy (four unfiltered exposures of 75 r each). On resumption of the saturated solution of potassium iodide a large bleb developed

medially in the left palm which disappeared when iodides were stopped. Culture of the bleb was negative for Sporotrichum, and within a week the swelling subsided and the patient was discharged as cured on Aug. 28, 1942.

The patient returned June 9, 1943 with a papillomatous lesion in the medial aspect of the left palm, which had been present for a week. De Beurmann, in one of his cases, noted that "a papillomatous patch of secondary infection developed in the neighborhood of the first lesion." Smears and culture from this area were negative for Sporotrichum. The histopathologic observations on biopsy, performed on June 21, 1943, were reported as follows by Dr. Wilbert Sachs:

". . . At the edge of the section the epidermis is acanthotic; the granular layer is increased, and the horny layer is also increased and densely laminated. At either side of the section the epidermis is missing, and considerable necrosis is present. Throughout the cutis is an intense cellular reaction with numerous small round cells and an occasional plasma cell. No parasites were found. . . ."

The patient was discharged on July 13, 1943 and has remained well since then.

SUMMARY

A case of solitary lesion of sporotrichosis (sporotrichotic chancre) is reported in which the patient had a nonsporotrichotic papillomatous growth in the palm of the same hand a year later. Although iodide therapy is specific in the treatment of sporotrichosis in cases in which there is an intolerance to iodides, roentgen ray therapy is of value.

Diagnosis of sporotrichosis without cultures is impossible, as the lesion in its various stages may simulate any of the diseases producing granulomatous reactions.

A FORMULA FOR CRYOTHERAPY FOR ACNE AND POSTACNE SCARRING

ISADORE ZUGERMAN, M.D., PHILADELPHIA

The purpose of this paper is to suggest a modified formula to be used in making carbon dioxide slush for the treatment of acne and postacne scarring.

The benefits, failures, indications, contraindications and methods of use have been discussed in detail by other authors.[1]

My study consisted of the use of slush treatment for acne and postacne scarring on 150 patients, ethyl acetate instead of acetone being used in its formula. The results of treatment were good, definitely paralleling those of Dobes and Keil.[1a]

The substitution of ethyl acetate for acetone was made for the following reasons:

1. A better and longer-lasting slush is obtained, which makes it easier to handle. Ethyl acetate (boiling point, 77 C.; specific gravity, 0.900), also a fat solvent, is similar in action to acetone (boiling point, 56.5 C.; specific gravity, 0.788) but is less volatile.

From the Dermatologic Service of Dr. A. Strauss, Jewish Hospital, Philadelphia.

1. (*a*) Dobes, W. L., and Keil, H.: Treatment of Acne Vulgaris by Cryotherapy (Slush Method), Arch. Dermat. & Syph. **42**:547 (Oct.) 1940. (*b*) Friedlander, H. M.: Failure with Cryotherapy in the Treatment of Acne Scars, ibid. **46**:734 (Nov.) 1942.

2. The odor of ethyl acetate is less objectionable to most patients because of a definite sharp fruity character. It is used commercially in manufacturing fruit essence.

The method of procedure is to grind with a mortar and pestle ½ pound (227 Gm.) of solid carbon dioxide and to add 1 drachm (4 Gm.) of precipitated sulfur. This is thoroughly mixed, and then ethyl acetate is slowly added until a semidry slush is formed. The consistency may vary according to individual desires and progress of treatment. It is always advisable to make a thinner mixture early in the treatment because the reaction is not so severe as when thicker mixtures are used. The slush is applied with the pestle, to which several layers of gauze have been attached to the grinding edge by means of an elastic band.

It is recommended that no moisture be allowed to contaminate the ethyl acetate, because it slowly decomposes and acquires an acid reaction. This phenomenon has never been a factor in causing untoward reactions.

There have been no unfavorable reactions directly traceable to the use of ethyl acetate instead of acetone in cryotherapy.

4234 Old York Road (40)

EPILATION BY ELECTRODESICCATION OF HAIRS OF THE SCALP INFECTED BY FUNGI

MAURICE J. COSTELLO, M.D., NEW YORK

Dermatologists have had the experience of finding it difficult to rid the scalp of the few remaining hairs infected by fungi after epilation by roentgen rays. Great difficulty is encountered in removing these infected hairs by manual epilation with tweezers because it is often impossible to grasp the hair which has broken off near or at the surface of the scalp or because it readily breaks under traction when held between the blades of the epilating forceps. Nevertheless, the Department of Health of the City of New York will not permit a child with ringworm of the scalp to return to his classroom if even a single fluorescent infected hair is found in the scalp.

During the past three years, I have overcome the difficulty in epilation by inserting the fine needle of the short wave high frequency current into the hair follicle alongside the infected hair. When the current is turned on, as the needle is withdrawn the infected hair is oftentimes attached to it. This operation should be performed in a dark room with the aid of the Wood fluorescent light. Complete destruction of the hair follicle does not always occur, and a normal healthy hair may later grow from the follicle. Even though as many as a dozen separated hair follicles were destroyed in this manner, the minimum loss of hair would be inconsequential and would not be noticed in the scalp, which is covered by thousands of hairs.

This simple method of destroying infected hairs will permit the return of children to school much earlier than if one had to wait for a similar result by any other method.

140 East Fifty-Fourth Street (22)

Abstracts from Current Literature

EDITED BY DR. HERBERT RATTNER

SULFATHIAZOLE OINTMENT FOR PREVENTION AND TREATMENT OF PYODERMAS OF NEWBORN INFANTS. CHARLES A. WEYMULLER and ELIZABETH J. ITTNER, Am. J. Dis. Child. **69**:283 (May) 1945.

This paper deals with 3,205 newborn infants, each of whom was anointed just after birth with 15 Gm. of 5 per cent sulfathiazole in an emulsion ointment base. This preparation was used in an attempt to prevent pustular infections.

Only 4 sporadic cases of pyoderma developed. However, most of these babies were discharged from the hospital seven to ten days after birth. The authors stress that pyoderma in infants is characterized by periods of low incidence. Such facts must be considered in evaluating this prophylactic procedure.

Of the 3,205 infants 49 were readmitted for serious illnesses which required full doses of sulfonamide compounds. In 43 instances the drug employed was sulfathiazole. No instance of sensitization to sulfonamide compounds was encountered. This observation seems to show a low sensitizing power of sulfathiazole in the newborn infant.

NELSON PAUL ANDERSON, Los Angeles.

THE TRANSFER OF PENICILLIN INTO THE CEREBROSPINAL FLUID FOLLOWING PARENTERAL ADMINISTRATION. WALSH MCDERMOTT and R. A. NELSON, Am. J. Syph., Gonor. & Ven. Dis. **29**:403 (July) 1945.

By dilution technics of bioassay, no penicillin was demonstrable in the cerebrospinal fluids obtained from 70 patients who had received penicillin in various doses by parenteral routes. The presence of neurosyphilis and, in 1 instance, of tuberculous meningitis did not alter these results.

With the use of an inoculation test for the presence of penicillin approximately 0.02 unit was demonstrable in the cerebrospinal fluid of patients who had received one or two intramuscular injections of 300,000 to 500,000 units of penicillin three to four hours previously.

The failure of the penicillin to appear in the cerebrospinal fluid in appreciable amounts is not due to the fact that it is bound to a high degree to nondiffusible elements in the serum.

The authors suggest that, as the immediate results from intramuscular injection of penicillin for syphilitic meningitis and other forms of neurosyphilis are so promising, it is unnecessary to use the intrathecal route for the treatment of these diseases. On the other hand, in the treatment of purulent meningitis it would seem that on the basis of the available information the administration of penicillin by the intrathecal route cannot be abandoned.

EXPERIMENTAL SYPHILIS IN DIFFERENT SPECIES OF NATIVE AMERICAN MICE. UDO J. WILE and STURE A. M. JOHNSON, Am. J. Syph., Gonor. & Ven. Dis. **29**:416 (July) 1945.

All five species of native American mice or their subspecies were found to be capable of harboring syphilitic infections after inoculations with Nichol's strain of Treponema pallidum obtained from rabbits. The infection was as readily carried by female as by male mice. On dark field examinations of all material from mice which proved infectious for rabbits no spirochetes were observed. In no instance were any syphilitic changes demonstrable in the inoculated mice.

EXPERIMENTAL SYPHILIS IN THE GOLDEN HAMSTER. UDO J. WILE and STURE A. M. JOHNSON, Am. J. Syph., Gonor. & Ven. Dis. **29**:418 (July) 1945.

Pooled emulsions of organs of golden hamsters infected by the intraperitoneal route with Treponema pallidum of the Nichol strain obtained from rabbits can be used to produce experimental syphilis in rabbits. Syphilis in hamsters seems to be similar to that which is found in white mice in that the infection remains unapparent. Results of control experiments were negative. The passage of syphilitic infection through the hamster did not increase the virulence of the infection in rabbits, as was noted in mice by the authors.

LATE NEUROSYPHILIS IN NORTH AMERICAN NEGROES AND WHITES. WALTER R. KIRSCHBAUM, Am. J. Syph., Gonor. & Ven. Dis. **29**:432 (July) 1945.

Clinical and postmortem observations on white and on Negro patients with dementia paralytica are compared. Dementia paralytica occurs, according to the ratio of syphilis, as frequently in the Negro as in the white population in this country. The average age of onset is younger in Negroes, owing to earlier infection. Stationary dementia paralytica in white persons tends to be more chronic and prolonged than in Negroes. More cases of atypical dementia paralytica are observed among Negroes because of concomitant vascular lesions.

In all its varieties, including atrophy of the optic nerve, tabes dorsalis in white patients does not differ from that in Negro psychiatric patients. Only statistics from large city hospitals can settle the question of its frequency among the general Negro population. Organic psychosis due to meningovascular syphilis combined with other disease is more frequently found in Negroes. A high percentage, 44 per cent, of syphilitic aortitis was found in both races. In at least 5 per cent of the cases of dementia paralytica the blood serologic tests elicited negative reactions at the onset, although the tests of the spinal fluid elicited strongly positive reactions at the same time. On the other hand, negative reactions to serologic tests of the spinal fluid together with positive reactions to blood tests have been rarely observed in untreated patients. This paper is concerned only with the Negro population in the United States. The rare incidence of late neurosyphilis among other Negro stocks is acknowledged.

REUTER, Milwaukee.

THROMBOCYTOPENIC PURPURA DUE TO MAPHARSEN. MARVIN SCHWARTZ and ELMORE C. VONDERHEIDE, J. A. M. A. **128**:657 (June 30) 1945.

A case of thrombopenic purpura after thirty injections of oxophenarsine hydrochloride is reported. The platelets in the peripheral blood are probably not destroyed but merely dislocated temporarily into the large capillary beds of the vascular tree, which have been rendered more permeable. No fatalities have been recorded thus far as a result of this complication.

DERMATITIS FROM WEARING APPAREL. LOUIS SCHWARTZ and SAMUEL M. PECK, J. A. M. A. **128**:1209 (Aug. 28) 1945.

Dermatitis has been reported to be caused by fabrics, such as silk, wool and synthetic fibers, by leather, artificial leather, furs, rubber and rubber-containing materials, such as rubber gloves, dress shields, girdles, socks, pajamas and brassières. Metal and metal alloys, used in jewelry and in eyeglass frames, wrist watches and watch straps, also have caused dermatitis. Plastics, used in spectacle frames, straps for wrist watches, garters and suspenders, have produced dermatitis.

In the majority of the reported cases of dermatitis due to the wearing of fabrics the eruption has been caused by the processed fabrics. Dermatitis among the wearers of fabrics is often caused by the finishes rather than by the dyes. The inner lining of shoes, as well as the backing, contains chemicals which may cause dermatitis. In most cases dermatitis from metallic jewelry has been attributed to nickel. Paraphenylenediamine has been the chief cause of dermatitis from fur.

The eruption begins at the place of contact with the offending material, usually five days or more after the garment has been worn. The patch test is the most practical method for demonstrating the actual cause of a contact dermatitis.

THE TREATMENT OF HERPES ZOSTER BY PARAVERTEBRAL PROCAINE BLOCK. THOMAS FINDLEY and REYNOLD PATZER, J. A. M. A. **128**:1217 (Aug. 25) 1945.

Spontaneous and permanent relief from pain was obtained by 4 patients with herpes zoster treated by infiltration of the appropriate sympathetic ganglions with procaine hydrochloride. Block of the regional sympathetic supply relieves herpetic pain by abolishing segmental vasospasm.

BORIC ACID. E. H. WATSON, J. A. M. A. **129**:332 (Sept. 29) 1945.

A boy aged 4½ months, with severe infantile eczema was treated with continuous warm wet dressings of saturated solution of boric acid applied to the entire body. By the second day of this treatment, the skin had improved and boric acid ointment was applied twice daily to all inflamed areas. Three applications were made, a total amount of ointment somewhere between 60 and 100 Gm. being used. Sufficient boric acid was absorbed in the twenty-four hour period after the first application to produce convulsions. Blindness and deafness followed. An intense and generalized erythema developed; this was so pronounced that the child was literally the color of a boiled lobster. The patient died three weeks following the onset of the boric acid poisoning. Watson believes that the use of boric acid preparations should be discouraged because of their limited usefulness and the real dangers of their accidental and of their intentional use. Boric acid is a poison.

X-RAY BURNS RESULTING FROM FLUOROSCOPY OF GASTROINTESTINAL TRACT. L. H. GARLAND, J. A. M. A. **129**:419 (Oct. 6) 1945.

During a gastrointestinal fluoroscopic examination by a physician each of 4 patients received serious and temporarily incapacitating burns of the skin over the lumbar area. A small portable x-ray unit was used. X-ray units which are portable and shockproof can be brought much closer to the patient than could the older, heavier, nonshockproof units. A lack of adequate distance between the x-ray tube and the patient's skin is one of the chief sources of danger. If adequate distance, reasonable voltage and low milliamperage, use of a filter, proper speed and dispatch in examination and dark adaptation of the eyes before the commencement of any fluoroscopic work are kept in mind, the average operator is not likely to cause any serious damage.

SKIN DIABETES: HYPERGLYCODERMIA WITHOUT HYPERGLYCEMIA. ERICH URBACH, J. A. M. A. **129**:438 (Oct. 6) 1945.

The average sugar level of the human skin is 58 mg. per hundred grams. A skin sugar level of more than 68 mg. per hundred grams is pathologic. The average ratio between skin sugar and blood sugar is 61 per cent. When the ratio is 70 per cent or more, "independent cutaneous glycohistechia" is present. The term "skin diabetes" is suggested to serve as a designation for the syndrome of a therapy-resistant disease of the skin (furunculosis, abscess of the sweat gland, eczema, pruritus), a high fasting skin sugar level together with a normal blood sugar curve and pronounced improvement of the dermatosis, as well as a fall in the high skin sugar level on a low carbohydrate diet sometimes in combination with insulin.

The high fasting skin sugar levels, the pathologic and characteristically diabetic course of the skin sugar curve following forcing of sugar by mouth and the return to normal of the fasting skin sugar level, as well as of the skin sugar tolerance curve with a low carbohydrate diet, notably in connection with insulin, indicate a connection between the clinical syndrome and a disturbance in the carbohydrate metabolism. Not only is sugar in the skin brought there by way of passive diffusion from the blood, but there is also an independent, intermediary carbohydrate

metabolism in the skin. "Independent cutaneous glycohistechia" should be regarded as an entity in no way related to the general sugar metabolism of the body and thus unrelated to ordinary diabetes mellitus.

BENZIDINE AS CAUSE OF OCCUPATIONAL DERMATITIS IN A PHYSICIAN. RUDOLPH L. BAER, J. A. M. A. **129**:442 (Oct. 6) 1945.

A physician suffered from a severe recurrent eczematous dermatitis on the hands and a milder dermatitis on the face. A test patch with benzidine powder produced a strong eczematous reaction. Each attack of dermatitis had started on a day when the patient had performed a benzidine test for blood in a specimen of stool.

HENSCHEL, Denver.

THE NONANTIGENIC PROPERTY OF BEESWAX. LESLIE N. GAY, J. Allergy **16**:192 (July) 1945.

The author investigated the possible contamination of beeswax by various pollens.

Microscopic examination of crude and filtered "mixed" beeswax revealed no pollens of trees, grasses or ragweed.

Scratch tests with 4 per cent crude and filtered beeswax–arachis (peanut) oil mixtures administered to 12 patients suffering from hay fever or asthma due to one or more varieties of pollens elicited negative reactions. Control tests with similar mixtures to which varying amounts of pollen extracts was added elicited positive reactions. Intracutaneous tests with 4 per cent crude and filtered beeswax-peanut oil mixtures, administered to 31 pollen-sensitive persons, elicited negative reactions.

In the author's opinion beeswax in peanut oil is nonantigenic and is an ideal medium for delaying the absorption of penicillin when administered subcutaneously or intramuscularly. He advises, however, that the beeswax not be kept in solution in a concentration greater than 4 per cent by weight.

MENDELSOHN, New York.

SYPHILIS IN INDUCTEES. JACOB ZELLERMAYER, J. Ven. Dis. **26**:194 (Sept.) 1945.

Among 5,000 men inducted into the armed forces suspected of having syphilis, 570 (11.4 per cent) were proved to be completely free of the disease. Most of these had been suspected of having the disease on the basis of a single blood test; this fact strengthens the concept that a positive serologic reaction alone does not establish the diagnosis of syphilis. Ten and fifty-six hundredths per cent were probably cured of their infection; 1.24 per cent had primary, 0.14 per cent had secondary, 48.84 per cent had early latent and 14.84 per cent had late latent syphilis; 12.98 per cent had complicated syphilis, chiefly cerebrospinal. There was considerable doubt concerning the diagnosis for an additional 6.3 per cent; this shows the need for careful study of the patient before beginning therapy for syphilis.

The group of probably cured patients had received more treatment and more regular treatment than those still having evidences of infection. Nearly 60 per cent of the seropositive patients in the group were found to be previously untreated and to have previously unrecognized infections.

REUTER, Milwaukee.

MYCOTIC INFECTIONS. J. G. DOWNING and N. F. CONANT, New England J. Med. **233**:153 and 181, 1945.

Downing and Conant review recent advances in mycotic infections in the light of the changes created by the war in the living habits of large groups of the population. Fungous infections are divided into four major categories: superficial mycoses, dermatomycoses, subcutaneous mycoses and systemic mycoses. In the first category are discussed tinea versicolor, erythrasma, trichomycosis, piedra and otomycosis and in the second category infections due to Trichophyton, Microsporon and Epidermophyton. Unfortunately, recent studies of and suggestions for the

therapy of tinea pedis have not produced as yet a standard method of treatment. Among the subcutaneous mycoses discussed are chromoblastomycosis, maduromycosis and sporotrichosis. Among the systemic are coccidioidomycosis, North American blastomycosis, South American blastomycosis, cryptococcosis, histoplasmosis and actinomycosis.

PEDICULOSIS CORPORIS AND LEG ULCERS. G. E. MORRIS, New England J. Med. **233**:180, 1945.

Morris lists approximately twenty-seven possible diagnoses offered by physicians to explain ulcers of the legs in the middle-aged patient. One, however, is overlooked. Pediculosis corporis is often the underlying cause of multiple ulcers of the legs.

FALSE-POSITIVE HINTON REACTIONS FOLLOWING CHICKEN POX. L. W. KANE and P. H. HENNEMAN, New England J. Med. **233**:407, 1945.

A review of the literature on the subject reveals only 1 questionable report, by Gunn in 1930. Of 22 unselected persons convalescent from chickenpox, 5 had positive Hinton reactions and 1 a positive Kahn reaction. In no case was these a positive Wassermann reaction. These results emphasize the need for a careful evaluation of each case before the patient is subjected to the psychologic trauma of a diagnosis of syphilis and to antisyphilitic treatment.

PLASTIC SURGERY UPON THE AXILLA IN CERTAIN CASES OF PERSISTENT BROMIDROSIS. K. KAHN, New York State J. Med. **45**:1555, 1945.

Kahn reviews the anatomy of the sweat glands and the pathology of bromhidrosis. He has observed a frequency of it as high as 40 per cent in Negro patients and between 6 and 10 per cent in white patients. The offensive axillary odor which persists regardless of hygienic measures is accentuated and becomes decidedly nauseating after intercourse, but only after an orgasm has been completed.

In cases in which the offensive odor failed to respond to soaps, deodorants and antisudorifics, the author has obtained satisfactory results from a blunt dissection and removal of all the gland-bearing subcutaneous tissue in an area previously mapped for the operation according to the number and distribution of the glands. The author's experience has been limited to the use of the sliding graft, which should be the preferred method.

DERMATOLOGIC ASPECTS OF POLIOMYELITIS. J. G. REYES, New York State J. Med. **45**:1673, 1945.

During the recent epidemic of poliomyelitis in New York, Reyes had the opportunity to observe the great frequency of hyperkeratinization in patients suffering from this disease. In 98 per cent of the cases hyperkeratotic lesions were located on both infrapatellar areas, on the anterior and lateral aspects of both ankle joints, on the dorsa of both feet, on both soles and on the malleoli. These lesions, resembling those encountered in cases of vitamin A deficiency, seemed to be proportional in severity to the severity of the poliomyelitis, their prominence disappearing with the abatement of the poliomyelitis. Therefore vitamin A deficiency may be considered as a possible predisposing cause of poliomyelitis. Further investigations are suggested as to the possibility of treating poliomyelitis with vitamin A.

RONCHESE, Providence, R. I.

RADON OINTMENT TREATMENT OF IRRADIATION ULCERS. ROBERT E. FRICKE and MARVIN M. D. WILLIAMS, Radiology **45**:156 (Aug.) 1945.

In 2 cases ulcers due to irradiation, of many years' standing, had undergone malignant change and were treated at Mayo Clinic by the application of petrolatum that contained radon and by highly filtered radium. Since 1930 Uhlmann has advocated the application of radon ointment in the treatment of radiodermatitis.

He has expressed the belief that the mechanism involved is the superficial effect of alpha particles. In the first case reported by Fricke and Williams, evidence of healing had occurred, but further treatment was necessary. In the second case, the ulcer healed completely.

HENSCHEL, Denver.

UNIVERSAL ALOPECIA. B. M. SCHOLDER and A. P. MORTON, U. S. Nav. M. Bull. **40**:348 (Aug.) 1945.

Scholder and Morton report a case of universal alopecia of eight months' duration in a 19 year old seaman. A neuropsychiatric examination revealed the patient to be suffering from a mild anxiety neurosis, which had been present for two years and had resulted from the shock of identifying the body of his father, who had committed suicide.

Physical, roentgenologic and laboratory examinations revealed normal conditions.

RODIN, South Bend. Ind.

ERYTHEMA NODOSUM AND OTHER COMPLICATIONS DUE TO INTRACUTANEOUS AND INTRAVENOUS FREI ANTIGEN INJECTIONS. C. E. SONCK, Acta dermat.-venereol. **21**:473 (May) 1940.

The cutaneous manifestation of venereal lymphogranuloma appears usually as an eruption resembling erythema nodosum, occasionally as an eruption resembling erythema multiforme exudativum and rarely as a morbiliform or other type of eruption.

Now that the intracutaneous and intravenous use of Frei antigen in the testing and treatment of venereal lymphogranuloma has become commoner, one can expect to find many more cases of lymphogranulomatous eruptions of the skin. The use of this method of treatment serves to produce the cutaneous manifestations, possibly through an allergic phenomenon.

The author describes 8 cases of erythema-nodosum-like eruption following treatment with Frei antigen and roentgenotherapy. In 4 of his cases there were other factors, such as rheumatic arthritis. In 2 of the cases uncomplicated by any other factors erythema-nodosum-like eruptions followed intracutaneous Frei tests. In 2 other cases the eruptions appeared following intravenously injected Frei antigen and were accompanied with a strong focal reaction in the one and hallucinations in the other. In 1 patient a progressive hyperchromic anemia developed resulting in death following an intravenous injection of Frei antigen. The author believes that in the latter case the therapy was a contributory factor.

PHOTOSENSITIVITY IN LYMPHOGRANULOMA INGUINALE: CLINICAL STUDY. C. E. SONCK, Acta dermat.-venereol. (supp. 6) **22**:1, 1941.

The photosensitivity of 400 patients with venereal lymphogranuloma, evenly divided between males and females, has been investigated. The results have been published in monographic form as an original and primary contribution. At the time of writing, only 1 report of this phenomenon had previously appeared (de la Cuesta), and this report explained the photosensitivity as being due to the antimony used in treatment of the disease.

The manifestations in the cases reported are divided into five stages: (1) subacute inguinal adenitis, (2) chronic inguinal adenitis, (3) chronic ulcer of vulva or penis (fistula of penis), (4) chronic proctitis and (5) genitoanorectal syndrome.

The solar eruptions are produced only by direct sunshine on exposed parts of the body. Attempts to produce the eruption by irradiation with a quartz mercury vapor lamp failed. Women are more susceptible than men. The eruption occurs in 60 per cent of women with chronic and in 30 per cent of women with subacute lymphogranuloma venereum and 12 per cent of men. Not all the exposed parts are equally susceptible. The eruption occurs in the following places, with decending frequency: (1) extensor surfaces of forearms and legs, (2) flexor surfaces of

forearms and legs, (3) extensor surfaces of arms and thighs, (4) flexor surfaces of arms and thighs, (5) neck, nape and sternoclavicular triangle and (6) abdomen, back, hips, face and backs of hands.

The eruption varies in appearance from erythematous pinpoint-sized papules to large urticarial wheals, 3 to 7 mm. in diameter, and is occasionally accompanied with a diffuse erythema of the affected areas. The eruption is frequently accompanied with moderate or severe pruritus and sometimes with a feeling of discomfort or restlessness. The more sensitive women patients complained of nervousness, nausea and oppression and occasionally of giddiness, headache, chills and numbness of the affected parts.

The photosensitivity appeared five to six weeks after the appearance of the first glandular symptoms and disappeared when the basic disease was cured. In the patients with subacute disease the photosensitivity appeared during a single summer. In the patients with chronic disease the photosensitivity lasted for several years, starting in the spring and disappearing in early autumn, becoming less intense year after year until it finally disappeared. This phenomenon often disappears after a radical operation, such as resection of the rectum. In 6 cases the photosensitivity persisted after all symptoms of the disease had disappeared.

Of the women with chronic lymphogranuloma venereum arthritis appeared in 33 per cent, conjunctivitis in 19 per cent and erythema nodosum in 16 per cent of those who were photosensitive. Of the nonphotosensitive patients arthritis appeared in 19 per cent, conjunctivitis in 7 per cent and erythema nodosum in 4 per cent. Intensely strong Frei reactions occurred in 32 per cent of those with photosensitivity and in 9 per cent of those without this phenomenon.

Investigation into the protein and lipid content of the blood serum, blood counts and urinary porphyrin did not reveal different values for photosensitive patients from those of nonphotosensitive patients.

ROBINSON, Washington, D. C.

ACRODERMATITIS ATROPHICANS OF THE FACE AND THE RIGHT UPPER EXTREMITY WITH FORMATION OF NODES. G. MIESCHER, Dermatologica **86**:233 (Oct.-Nov.) 1942.

Four years before seeking treatment a 30 year old man noticed transient bluish red discoloration and edematous swelling below the eyes, of the middle part of the face, of the right elbow and, at a later date, of the right hand and forearm. When seen he complained of rheumatic pain in the right thumb and other joints of the right upper extremity.

The nose, lips and cheeks were decidedly disfigured and of a pale, purplish red hue. The epidermis was thin and somewhat atrophic. The right hand appeared large, and the right thumb was twice the width of the left; the skin showed the same changes as that of the face. A streak of cyanotic discoloration extended from the dorsum of the right hand along the ulnar border to the elbow. Along its course many platelike infiltrations could be felt. The roentgenogram revealed normal bones of the hands and moderate enlargement of the sella turcica. The histologic picture was typical.

The extensive process and the pseudoelephantiasic changes are unusual.

ALOPECIA AREATA MALIGNA TOTALIS: CURE WITH PERANDREN. W. STALDER, Dermatologica **86**:262 (Oct.-Nov.) 1942.

A 60 year old woman showed in 1940 almost complete loss of hair due to alopecia areata maligna. For a year no growth of new hair was observed in spite of treatment with ultraviolet rays, arsenic, acetylcholine, injections of estrone, and application of ointment and lotions. When twenty injections of 5 mg. of testosterone propionate were given in 1941, the hair started to grow in more densely than it had been before the disease.

HELEN O. CURTH, New York.

Society Transactions

LOS ANGELES DERMATOLOGICAL SOCIETY

A. Fletcher Hall, M.D., *Chairman*

Clement E. Counter, M.D., *Secretary*

Jan. 9, 1945

A Case for Diagnosis (Acanthosis Nigricans?). Presented by DR. ANKER K. JENSEN.

A. S., a white woman aged 67, has hypertensive blood vascular disease, with a blood pressure of 188 systolic and 100 diastolic. There is disease of the gallbladder, evidenced by recurrent attacks of pain in the upper part of the abdomen and by roentgenologic examination of a nonemptying gallbladder. About five months ago she noticed a few pigmented areas developing on the sides of her neck. This has gradually spread, until at present both sides and the front of her neck show a mottled pigmentation. Some of the areas are a light brown and others a deeper brown, shading into a dark brown and black. The pigmentation does not extend entirely around the neck in the back. She says that she has not used local applications of cosmetics or other preparations, such as ointments or lotions.

DISCUSSION

DR. KENNETH STOUT: I did not arrive at a satisfactory diagnosis. I thought that the eruption might be acanthosis nigricans.

DR. HAL E. FREEMAN: I believe this is a case of argyrosis. The patient said that she had not used nose drops but that she had used eye drops about the same time the pigmentation developed. She did not know what these eye drops were, but they might have contained silver.

DR. SAMUEL AYRES JR.: I have seen a number of cases of localized argyrosis in the eyes from silver preparations, but I doubt that it is possible to use silver in the eye and get a deposit on the neck and still not show any in the eye. This may be pigmentation from some sort of cosmetic cream. She may have used something with mercury in it, but if that is the explanation for this woman's cutaneous disease why should the pigmentation be limited to the neck and not be present on the face? Also I should like to consider the possibility of a very early acanthosis nigricans. The pigmentation has been present only six months, and it is quite possible that there may be more roughening in the future. There is in this case a definite roughening, not exactly characteristic of acanthosis nigricans or of cutaneous tags, but all around the neck and on the chest are some peculiar little papules, some of which show slight pigmentation. I do not think that one could make a definite diagnosis at present from the clinical picture, but it looks to me more like acanthosis nigricans than anything else I can think of.

DR. W. H. GOECKERMAN: One cannot entirely exclude pigmentation due to mercury in face cream just because it is around the neck. Several years ago I reported a series of cases of pigmentation due to face cream in which the mercury in the cream was the causative agent. The patients had used it for years. They all had most of the pigmentation around the neck. I think that a biopsy is indicated. If it were found that particles of mercury could be demonstrated in the skin, it would clinch the diagnosis. Further study of the patient's history might help.

DR. ANKER K. JENSEN: I first thought that the pigmentation was due to the local application of some cosmetic, but there is no history of contact with or of the ingestion of any drug. She refused to allow a biopsy. There is a possibility of early acanthosis nigricans.

Glomus Tumor. Presented by Dr. Anker K. Jensen.

F. V. F., a white man aged 58, thirty-one years ago noticed some tenderness on pressure over the right thumb nail. This tenderness has gradually increased in severity. The thumb became so painful in 1927 that it was operated on. No improvement took place after the operation. The right thumb has never been acutely inflamed. Now there is severe acute pain on the lightest touch to the area over the medial side of the base of the right thumb nail. He has developed the habit of carrying the thumb in the palm and protecting it with his fingers. There is a deep red lesion, 3 mm. in diameter, at the base of the nail, where the tenderness seems to be the greatest.

DISCUSSION

Dr. Rogers F. Wakefield: I should like to thank Dr. Jensen for presenting this case today, for I have seen this lesion clinically only once before. The history of tenderness and the appearance of the lesion suggest glomus tumor. I agree with that diagnosis.

Black Hairy Tongue. Presented by Dr. Anker K. Jensen.

C. J. D., a white man aged 61, has been having a dry sore throat for the past three months. During that time he has been using different kinds of cough drops and candy type lozenges to relieve coughing. At times he has gone to sleep with such a cough preventive on his tongue. The posterior midportion of the tongue is covered with a dark brown overgrowth of filiform papillae, just anterior to the circumvallate papillae.

No fungous filaments were present in an extemporaneous preparation for direct microscopic examination.

DISCUSSION

Dr. M. E. Obermayer: The case was a good example of lingua nigra. However, as pseudo black tongue, which is produced by fungi, may have an identical appearance, the possibility of fungi being present should be considered. The relatively short duration of the disease is in favor of the fungus-produced discoloration of the tongue.

Dr. Samuel Ayres Jr.: It is interesting that this man had been holding cough tablets in his mouth for many months because of a chronic sore throat. That is one of the etiologic factors described in connection with black hairy tongue. I do not know what the mechanism is that produces a hairy tongue from the use of cough lozenges. Probably there is some chemical irritation of the papillae. I think that this would be an interesting case to report on later, after cessation of the use of cough drops with no other treatment.

Dr. Nelson Paul Anderson: If black hairy tongue were due to cough drops, one should see many more cases. This statement is not meant to deny the chemical origin of such a disease.

Dr. M. E. Obermayer: Pseudo black tongue is sometimes caused by a streptothrix and at other times by Microsporon minutissimum. Dr. Weidman was able to produce the disease in a monkey.

Dr. Anker K. Jensen: I believe that in this case one has an illustration of black hairy tongue due to the chemical irritation of the cough drops that have been used. No fungous filaments were present in the specimens examined.

Squamous Cell Epithelioma of the Lower Lip. Presented by Dr. Hal E. Freeman.

F. R., a man aged 38, a pipe welder, smokes cigarets and drinks liquor moderately.

A "callus" began on the middle portion of the lower lip, two years ago. One year ago while welding he was burned by hot slag on the middle portion of the lower lip. The present tumor has gradually developed to its present size in the past year.

The lower lip is thickened. There is an ulcer in the middle of the lower lip, on the mucous membrane, approximately 13 mm. in diameter, and this overlies a firmly and deeply infiltrated area 25 by 13 mm.

The Kolmer and Kline reactions of the blood were negative.

DISCUSSION

DR. IRVING BANCROFT: I do not see why this tumor could not be removed with a cautery.

DR. HAL E. FREEMAN: Slag is a chip of hot metal or rust which flies from the metal as it is burned by the welder's torch.

DR. IRVING BANCROFT: I think that this is indirectly an industrial case. It is similar to some of those cases of cancer among primitive races caused by the carrying of hot utensils on the abdomen.

DR. CLEMENT COUNTER: I think that this tumor can be removed, and my opinion is that it should have been removed some time ago. I am not at all clear about its connection with compensation. This type of case seems to me much like one of the knotty problems of compensation work. The patient and the insurance company want an opinion. How does one know that there was not a cancer there before the slag hit his lip? That point has to be established.

DR. A. FLETCHER HALL: He admits that a callus was there before he was hit by the slag.

DR. SAMUEL AYRES JR.: I agree with Dr. Counter. Here is a person with a sensitive lower lip. It crusts and peels with sunburn. That is the kind of lip on which cancer will develop. The patient admits that he had a "callus," which evidently antedated the slag burn. I do not think that this case involves a problem of compensation. I saw a man some time ago with an ulcer on his lip, which he said was due to a slag burn. A dark field examination revealed spirochetes, and the lesion was a typical chancre. I certainly believe in giving the man the benefit of the doubt, if there is one, but I do not see how there can be one when he admits having a "callus" before the alleged trauma. I think that it is a prickle cell epithelioma. I would use the high frequency cutting current widely and deeply.

DR. J. WALTER WILSON: The best cosmetic result can be got by incision with a cold knife rather than by red hot cautery.

DR. FRANKLIN BALL: One must consider what treatment will be necessary after the lesion on the lip is removed and what metastatic lesions may develop. One may grossly understate the necessary treatment when one says simply that this lesion should be removed. A great many considerations are necessary when one outlines the course of treatment in this case. All this has bearing on the industrial responsibility.

DR. NELSON PAUL ANDERSON: I do not believe that the industrial aspects of this particular case should be dismissed too readily because of the fact that this man has a thin, sensitive type of skin. In the first place, one does not know that heat has a definite effect, as Dr. Bancroft mentioned. In the second place, when this man goes out in the sun, an actinic cheilitis develops. The conjunctivitis in welders is similar to that produced by the ultraviolet rays from a lamp. Wearing goggles protects his eyes, but his lips are unprotected. The light from the welding arc can definitely aggravate a preexisting lesion.

DR. A. FLETCHER HALL: I think that as far as the industrial responsibility is concerned in this case it could be argued all night as to whether or not one burn with slag or from some other source is likely to set up a malignant process on previously conditioned skin. I believe that the Industrial Accident Commission would find this case to be industrial without a doubt, although there is reasonable doubt in my mind. I agree with Dr. Wilson that the best cosmetic result could be expected from excision of a V-shaped wedge and primary suture. I think that radiation would not give as good a result.

DR. JOHN D. ROGERS: The history reveals that this man uses cigarets. The particular type of skin and the history of a little callus present for two years would

make me undecided as to whether or not the slag had anything to do with causing the lesion. I favor the opinion that the type of skin and the use of cigarets are the causative factors.

DR. A. FLETCHER HALL: The history of being "hit by something" is so common in retrospect that it is dangerous to accept that story as bearing on the causation. Last month a man was shown before this society who "thought" that he had been burned on the arm and that a lesion had developed there subsequently. Welders are constantly being struck by burning particles and malignant tumors seldom develop; unless the injury in question was reported by the patient at the time it is difficult to evaluate.

DR. ANKER K. JENSEN: I think that the lesion should be removed surgically by cautery. I think that any squamous cell epithelioma of the lower lip is best removed surgically and the lip subsequently treated with irradiation.

DR. HAL E. FREEMAN: In determining the answer to the question of whether or not this is occupational or would be so considered by the Industrial Accident Commission, I was eager to have the opinions of the members. This man did report to the field hospital of his company on Dec. 1, 1943, with a slag burn on this site, and his visit is on record. He himself was fair enough to say that he had had a callus for one and a half years previously, but this was not placed on record at the field hospital. It would not be dishonest to say that this tumor, if not caused by this occupational trauma which is recorded, was possibly aggravated by it. In regard to therapy, if I had what I wanted with which to treat this man, I would consider interstitial radium needles. I have treated cancers of the lip that way with excellent results. I do not agree with the speakers who feel that this tumor should be excised. I think that it will respond well to roentgen rays with proper filtration, and I will show the result of this therapy at a future meeting.

A Case for Diagnosis (Atrophic Lichen Planus?). Presented by DR. A. FLETCHER HALL.

E. P., a white woman aged 38, first noticed a group of closely set papules on the ulnar surface of each forearm ten years ago. These patches have remained, and new patches have appeared on the legs and the trunk. They have never itched. New patches of lesions have appeared in the past two years, and these are much more prominent in the past five months. No area once involved has ever cleared.

The ulnar aspect of each forearm, just below the elbow, shows an oval half-dollar-sized group of closely set pinhead-sized papules. Each has light brown pigmentation. The lateral aspect of the left leg has a half-palm-sized, slightly depressed area of light pigmentation and minimal papular elements. The posteromedial aspect of the left thigh and the right side of the chest at the level of the fourth rib show oval palm-sized groups of pinhead-sized pale discrete papules, which are accentuated by stretching the skin. These patches show a tendency to peripheral activity with central clearing. The dorsum of the right hand and wrist show scattered discrete pinhead-sized pale pink papules, each having a depressed glistening center.

The Wassermann reaction of the blood was negative five months ago. The biopsy slide presented with the patient shows only atropic changes in the epidermis and corium and is considered not satisfactory because it probably is not a representative specimen.

The patient received six or eight roentgen ray treatments from a dermatologist in Portland, Ore., several years ago. There was improvement but not complete clearing.

DISCUSSION

DR. CLEMENT COUNTER: The diagnosis that suggested itself to me was granuloma annulare with disseminate lesions. Obviously, if that diagnosis were to be proved, it would be necessary that some lesions, at least, were slightly raised. In this case all are flat. On the backs of the hands are two or three possibly beginning lesions of that disease, and the patient states that these are the newest lesions.

DR. NELSON PAUL ANDERSON: I agree with Dr. Counter's diagnosis.

DR. SAMUEL AYRES JR.: I thought that the disease was a disseminated granuloma annulare. It is rather a different picture from the localized lesions commonly seen on the hands. In this case I think that if one palpated most of the areas one could detect some definite infiltrations.

DR. M. E. OBERMAYER: I cannot agree with the suggestion of granuloma annulare. I thought that Dr. Hall's diagnosis was clinically well founded, as there was definite atrophy. However, the section showed none of the features of lichen planus. Dr. Couperus, with whom I saw the patient, suggested a superficial form of localized scleroderma. After having seen the slide, I am inclined to agree with his suggestion.

DR. A. FLETCHER HALL: Three years ago the patient had five or six roentgen ray treatments by a dermatologist in Portland. This was followed by slight improvement. I feel that the specimen I took for biopsy was not a good one; if I had chosen a different location from which to take the specimen, it might have had more characteristic changes.

A Case for Diagnosis (Lupus Erythematosus?). Presented by DR. NELSON PAUL ANDERSON.

According to M. J., a white woman aged 50, the present eruption around her eyes started six months ago following a "face peel." She was employed by Douglas Aircraft Company, working under fluorescent lights for fifteen months. During all this time her eyelids were puffy and swollen and the eyeballs were sore and sensitive. Often she applied hot and cold compresses to her eyes for relief. This past summer she took "ultraviolet" treatment and began to get deep circles under her eyes. Following this she had the "face peel."

She has nocturia—micturition two or three times or even every hour—and she has been advised that the walls of her bladder are thickened and enlarged. She had arthritis in her left shoulder and arm while working at Douglas. Late this summer her hands and feet were involved with arthritis. Recently the hips have become involved. She has taken many sun baths.

There is a symmetric purplish, violaceous discoloration of the upper and lower eyelids. There is arthritis in the spine and in the small joints of the fingers, evidenced by enlargements of those joints. There is no evidence of involvement of the muscles in the shoulder girdle.

The hematologic examination showed 16.9 Gm. of hemoglobin per hundred cubic centimeters; 5,260,000 erythrocytes and 3,800 leukocytes, with 61 per cent neutrophils, 32 per cent lymphocytes, 5 per cent monocytes and 2 per cent eosinophils. Platelets were normal. Erythrocytes were normal in shape and size.

DISCUSSION

DR. KENNETH STOUT: My only suggestion is that some substance used in the "face peel" sensitized the skin around the eyes and that what is seen now may be an actinic effect. I think that it would be a good plan for the patient to wear dark glasses to protect her eyelids.

DR. M. E. OBERMAYER: The leukopenia makes me consider the possibility of lupus erythematosus. Such a diagnosis would be in line with Dr. Stout's remarks about the precipitating effect of the "face peel."

DR. CLEMENT COUNTER: In the history of the onset of this "accident" last summer it is stated that the patient had a rather severe erythema for some time, and it is greatly improved over what it was then. This calls to mind a consultation I had a few weeks ago with another woman who had a similar reaction. Accompanying my patient was the woman who did the "peel" procedure. She was emphatic in her statement that this was the first time she had had this type of accident in sixteen years. I am surprised that persons doing such "face peel" procedures do not have more trouble than they do. It seems to me that the

patient I saw could easily have the same appearance as the patient presented here tonight when she gets that far along in the resolution of the reaction to the "face peel."

DR. SAMUEL AYRES JR.: I should not be at all surprised if this discoloration were a form of scar tissue. It has been said that when these chemical "face peels" are used to remove pitted scars there is scar tissue formed which more or less makes the other scars inconspicuous by comparison. I am wondering whether a section might not show changes analogous to a subkeloidal condition which cannot be palpated but which might give rise to this erythema. The margin between the production and the nonproduction of keloids from such chemical "peels" may not be large. Perhaps this discoloration is a subkeloidal scar in which a permanent increase in the small blood vessels or some new formation of fibrous tissue has taken place. The redness may gradually disappear, and there may be more scarring. It is too bad that some legal action cannot be taken to prohibit this type of procedure by nonmedical practitioners. There are a number of women doing this sort of work, and they are producing some bad results. They all seem to have the same procedure of applying chemicals and adhesive tape and leaving them on all night. Apparently the Board of Medical Examiners has no control over the situation, but it seems that there should be some way to attack the racket.

DR. A. FLETCHER HALL: I questioned this woman regarding the "peel," and she did not report a violent reaction to it. I could not get the history that there was deep exfoliation. She said that the swelling of the lids had been there for years. She ascribed this to "kidney trouble" which she has had for years. Her complaint seemed to be an indescribable sensation in the affected areas, as though there were "adhesions inside the eyelids." From the appearance of the rest of the skin, it did not look as though much damage had been suffered, and I was doubtful as to whether there was any connection between the "face peel" and her present complaint. In view of the arthritis and the swelling of the eyelids, I could not help thinking of the possibility of trichinosis, and I think that an intradermal test with the trichinella extract should be used.

Lymphatic Metastasis of a Cutaneous Epithelioma. Presented by DR. NELSON PAUL ANDERSON.

A. B., a white woman aged 62, has had a lesion on the left cheek for about eight years. When she was examined four years ago, she had a small, pea-sized, ulcer on the left cheek about 2 cm. from the left ala of the nose. Its base was thickened, but no pearly margin was present. Two years ago she was examined and was said to have a peculiar type of basal cell epithelioma.

Now there is a prominence of the lymphatics in the cheek for about 3 cm. around the site of the original indurated pea-sized ulcer. This ulcer is now healed in response to radium treatment. A biopsy specimen shows cancer cells, apparently of the basal cell type but actually somewhat different from the cells usually present in ordinary basal cell epithelioma. There is a lymphatic dissemination of the basal cell type.

DISCUSSION

DR. M. E. OBERMAYER: The section was interesting because it showed the strands of cancer cells in the lymph spaces.

DR. NELSON PAUL ANDERSON: The second biopsy specimen which was shown tonight was the one taken from the edge of the lesion in the left malar region.

DR. W. H. GOECKERMAN: I wish to ask Dr. Anderson whether he believes that this is an unusual type of epithelioma, viewing it now in the light of repeated biopsy examinations. It is an unusual way for a cutaneous cancer to spread.

DR. HAL E. FREEMAN: There is already a radiodermatitis present as evidenced by the telangiectasia and atrophy. I believe that this will enter into the consideration of future treatment.

DR. NELSON PAUL ANDERSON: In retrospect, the original lesion was one of those peculiar pearly white, button-like epitheliomas one occasionally sees. It is

impossible to state from clinical examination whether such a lesion is a basal cell or a prickle cell epithelioma. Usually radiation therapy is given to see how the lesion responds. Tonight this entire area of pearly white appearance looks as if procaine hydrochloride had just been injected. However, it has slowly and gradually developed over the past year and a half. Definitely this is not a so-called morpheaform epithelioma. It is an example of local lymphatic metastasis of a tumor which histologically resembles a basal cell epithelioma more than any other type of epithelioma. I have never seen this type of local lymphatic metastasis in any basal cell epithelioma. However, this patient has been seen by a physician with considerable experience with cutaneous cancer, who says that he has seen 3 similar instances. Frankly, I feel I am not qualified to make any comments on further treatment. The physician who has seen her in consultation feels that she should have radium needle implants.

CHICAGO DERMATOLOGICAL SOCIETY

Lester M. Wieder, M.D., *President*

Marcus R. Caro, M.D., *Secretary*

Jan. 17, 1945

A Case for Diagnosis (Vincent's Infection?). Presented by EDWARD A. OLIVER.

A white woman, aged 42, presents on the buccal mucosa of the lower lip two oval-shaped infiltrated ulcers. She states that about five weeks ago the lesions began on the left side of the lower lip as a "canker" sore. She bit this, and the ulceration began to increase in size and extent. The lip is swollen, painful and tender to the touch. There are no palpable glands in the submaxillary or submental region. The dark field examination did not reveal spirochetes. The Wassermann and Kahn reactions were negative, and a smear was negative for Vincent's organisms.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I do not know just how to classify these ulcers. I have seen similar ones, and I have vacillated between Vincent's angina and erythema multiforme. I believe that there is a form of necrotic aphthous ulcer that is rather similar too. I have no suggestions for treatment.

DR. CLINTON W. LANE, St. Louis: The ulcers in the mouth have necrotic dirty bases with surrounding inflammatory zones and appear much like the ulcers produced by Vincent's organisms. The patient has been adequately treated for Vincent's infection, and despite the few fusiform bacilli which are still present the eruption is probably not a spirochetal infection. On being questioned the patient admitted that for the past few months at frequent intervals she has been taking a proprietary drug for the relief of headache. The present ulcers may be the manifestation of a drug eruption.

DR. MAURICE OPPENHEIM (by invitation): I think that the eruption is a primary lesion of pemphigus. Another case presented this afternoon impressed me as being one of an initial lesion of pemphigus vegetans. Such lesions sometimes appear six months to a year in advance of the cutaneous eruption, as I stressed several times in the meetings of this society and in some of my publications concerning primary lesions of pemphigus. I used to consider all such lesions as suggestive of pemphigus, particularly if they did not respond to treatment. In erythema multiforme the lesions of the mucous membranes of the mouth have a much more inflammatory character.

DR. STEPHAN EPSTEIN, Marshfield, Wis.: This patient relates that the lesion in the mouth started as a "canker" sore about five weeks ago. She bit it, and then the stomatitis developed. She has had "canker" sores three or four times a year.

This woman reminded me of a patient of mine with a similar picture of ulcerative stomatitis. Last year the attack started after Christmas, and this year, before. She had been eating peanuts. I wonder if in this case one should not be on the lookout for an allergy to nuts or candy which might have brought on the attack around the holidays.

DR. MINNIE OBOLER PERLSTEIN: I should like to offer a diagnosis of periadenitis mucosa necrotica recurrens of Loblowitz and Sutton. Of the last 4 patients I have seen with this disease, 3 improved with heavy vitamin B therapy. Clinically, all presented the symptoms seen in this patient, except that in some instances there were more lesions on the buccal mucous membrane. The syndrome of recurrent painful necrotic aphthous lesions which heal with scarring is characteristic of the disease of Loblowitz and Sutton.

DR. S. W. BECKER: I wonder whether there may not be a factitial element in this case. The patient said that she had used silver nitrate for a long time. I wonder how much of this irritation is due to the irritative treatment.

DR. EDWARD A. OLIVER: I am not at all convinced that any one has made the correct diagnosis. The only drug that the patient has taken has been one containing acetylsalicylic acid, acetophenetidin and caffeine, which she occasionally takes for headaches. This lip is painful, and I do not believe that there is any factitial element present. In March she was seen by her family physician, who made a dark field examination, had a Wassermann test made and examined the lesions for Vincent's organisms, all with negative results. Since then I have had a Wassermann test, two dark field examinations and two examinations for Vincent's organisms made without finding anything. Another examination, made by Dr. James H. Mitchell, revealed hemolytic streptococci in pure culture. The lip is definitely infiltrated and the linear ulcers are rather deep. This patient is entirely well now after having had four roentgen treatments of 160 r and boric acid compresses.

Fox-Fordyce Disease. Presented by DR. THEODORE CORNBLEET and (by invitation) DR. H. C. SCHORR and DR. DAVID COHEN.

J. M., a student nurse aged 18, suddenly began to have an eruption twenty days ago. The changes of the skin are in the axillas and on the pubis. The lesions are small follicular nodules. The background of these shows a faint erythema. There is severe itching. The last menses were scanty but at the predicted time. Previously the flow was more profuse. Nothing else of significance was elicited from the past or present history. The patient is presented because of the recent and sudden onset of the eruption and to ask suggestions as to therapy.

DISCUSSION

DR. FRANCIS W. LYNCH, St. Paul: I have no therapy to suggest. This patient's menses had always been normal until the last two months; since then the flow has been noticeably scant. I do not know the nature of the endocrine relationship, but I think that there is some such association in this disease.

DR. MARCUS R. CARO: In addition to the location on the breasts and pubic area, she had a patch of the eruption on the neck and beneath the shoulder strap on the left side. The lesions suggested the presence of an underlying seborrheic factor. I suggest the use of a 40 per cent sulfur ointment as a therapeutic test.

DR. THEODORE CORNBLEET: I have tried giving various types of endocrine products in the treatment of the Fox-Fordyce disease without achieving any degree of success. Estrogen, if it had any effect, intensified the itching. I am convinced that the correct therapy does not lie in the direction of the estrogens. It is possible that the male sex hormones would be more effective. I have tried them in small doses, but so far they have been of no avail. I intend to try them in much larger doses to counterbalance the assumed excessive female sex hormones present in this disease. I have encountered this disease more commonly in Negroes than in white patients. It is noteworthy, too, that Negro subjects have more apocrine glands

than do others. Furthermore, these structures are more numerous in women. It is suggestive, therefore, that the number of apocrine glands naturally occurring in a group of persons determines the incidence of Fox-Fordyce disease in it. My special reason for presenting this patient with an entity that is not rare was the recent onset of the cutaneous changes and the immaturity as yet of the lesions.

Melanoma of the Heel. Presented by DR. HERBERT RATTNER.

The patient, a white woman aged 55, complains of a lesion on the right heel of six years' duration but with a rapid increase in size in the past two months. The lesion consists of a nodular tumor, the size of a silver dollar, involving the right heel. The tumor presents a bluish black pigmentation and ulceration at the periphery. The patient states that a piece of tissue was removed one year ago. The case is presented for therapeutic suggestions.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: I have no therapeutic suggestions, but I think that this case is a good illustration of the fact that a considerable number of malignant melanomas arise from acquired pigmented lesions. From reading the textbooks one gets the idea that most melanotic lesions arise from pigmented moles. It is my opinion that an equal number will arise from acquired pigmented lesions. In 17 cases of malignant melanoma which I have studied and in 13 of which the diagnosis was proved by biopsy, about half the neoplasms arose from acquired lesions. In most of them there were pigmented lesions of the senile type on the back or face, but some arose from other lesions. I think a malignant melanoma that arises from a senile lesion is relatively benign, as this one today is. This woman has had it for six years. Acquired pigmented lesions that undergo malignant change in young people are highly malignant. I do not think that amputation now will do any good, but I think that it is the treatment of choice.

DR. S. W. BECKER: I am glad to have Dr. Nomland make that statement. I, too, thought that most melanomas that are acquired develop from a lesion called lentigo maligna. One never knows how long the patient has had this type of lesion. I do not believe that amputation is the treatment of choice. There is one type of operation performed on some patients in which the lesion is removed up into the leg and thigh, including as nearly as possible the lymphatic channels that drain this area. The lymph nodes are dissected from both the femoral and the inguinal regions. It seems to me that that operation would give a reasonable chance of removing the entire process, and, also, if she does have a local recurrence the chances are that it would not spread so rapidly if a great deal of lymphatic tissue has been removed.

DR. E. P. LIEBERTHAL: I suggest radium therapy before surgical intervention is attempted to block off the lymph and vascular channels.

A Case for Diagnosis (Angioma Serpiginosum?). Presented by DR. HERBERT RATTNER and (by invitation) DR. H. RODIN and DR. M. S. KAGEN.

A 70 year old white man had a compound fracture of the right tibia twenty-three years ago, followed by osteomyelitis in 1934. During the past six months a dermatitis appeared on the right leg, which has large varicosities. Seven weeks ago, bright red papillary lesions having serpiginous borders and central clearing appeared on the buttocks, in the lumbar area and on the lateral aspects of both thighs. The eruption was bilateral and symmetric. During the past three weeks, the redness and papillary lesions have subsided, leaving suggestions of atrophy. The Kahn reaction was negative. The patient believes that he had similar lesions during childhood.

A histologic specimen is presented.

DISCUSSION

DR. PAUL A. O'LEARY, Rochester, Minn.: I believe that this patient has purpura annularis telangiectodes as described by Majocchi. The patient not only has purpuric lesions but has, in addition, annular telangiectatic plaques with atrophic centers. The unusual feature is the presence of the lesions on the lower part of the abdomen.

DR. OTTO H. FOERSTER, Milwaukee: I agree with the diagnosis of purpura annularis telangiectodes, or Majocchi's disease, as offered by Dr. O'Leary. I do not think that it is angioma serpiginosum because there is too much pigmentation and atrophy, considering the comparatively short duration of the disease, and primary angiomatous lesions are absent.

Exudative Dermatitis (?). Presented by DR. E. P. LIEBERTHAL and DR. I. M. FELSHER.

The patient, a white man aged 36, presented himself at Mandel Clinic of Michael Reese Hospital one month ago with the following history: On March 10, 1943, flat, pea-sized, dark red, sharply outlined lesions appeared on the tip and alae of the nose and on the glans penis and surrounding the urethral orifice. In the course of two months pea-sized, dark red, sharply outlined papular lesions appeared on the forehead, and dark red, scaly, nodular lesions, from the size of a dime to that of a quarter, on the right cheek, the dorsa of the hands, the flexor and dorsolateral surfaces of the forearm and on the entire surface of the glans penis. The lesions on the glans penis, with the exception of the periurethral area, have disappeared completely.

The history reveals that the patient resided for one year, 1939, in British Honduras. He admitted sexual intercourse with native women. In 1942 on the basis of one strongly positive Kahn reaction, his family physician treated him for syphilis with twenty-five injections of neoarsphenamine and the same number of injections of a bismuth preparation administered intramuscularly. On completion of this course of treatment he was pronounced cured of syphilis because of repeatedly negative complement fixation and precipitation reactions.

Pea-sized dark red papular lesions are also present on the scalp. The nodular lesions on the right cheek and occasionally on the forehead reveal exudation.

The Wassermann, Kahn and Eagle reactions have been repeatedly negative. The smears of material from the nose and the serum from a punctured nodule failed to reveal the presence of Hansen's bacilli. The smears from the exudative lesions revealed hemolytic Staphylococcus albus. The examination of the blood showed: erythrocytes, 4,000,000, and leukocytes, 6,800, with a differential distribution of 42 per cent polymorphonuclear neutrophils, 40 per cent lymphocytes, 8 per cent eosinophils, 9 per cent monocytes and 1 per cent basophils. Determination of blood chemistry revealed nonprotein nitrogen 86 mg., uric acid 7.1 mg., glucose (fasting) 67 mg. and total proteins 6.2 Gm. per hundred cubic centimeters. The basal metabolic rate one week ago was — 17.5 per cent. The patient had malaria in 1939 while in British Honduras and an intestinal infection which was followed by nephritis.

He has had extensive dermatologic therapy in the last three years which failed to make any impression on the lesions. We have been unable to accomplish any measure of success with various forms of therapy and would appreciate therapeutic suggestions.

DISCUSSION

DR. LOUIS H. WINER, Minneapolis: On histologic section the connective tissue showed areas in which the cells appeared foamy. I suggest another biopsy, with staining for fat. The disease may be an extracellular cholesterosis.

DR. MAURICE OPPENHEIM (by invitation): I observed this patient two years ago with a similar picture. The lesions were on the hands and arms. I made a diagnosis of dermatophytosis, and today I still think that my diagnosis is right.

I believe that the disease is now a disseminated deep type of dermatophytosis. The histologic observations do not speak against that diagnosis. I think that the patient should be treated with injections of trichophytin.

DR. S. ROTHMAN: May I ask whether the possibility of a drug eruption has been ruled out with certainty?

DR. E. P. LIEBERTHAL: The history reveals no ingestion of drugs. The histologic structure is typical of exudative dermatitis; however, one has to consider the possibility that previous roentgen therapy may have altered the original architecture of the tissue. Perhaps at a later date this might revert to the original structure. No significance can be attached to previous antisyphilitic therapy, because this was given on the basis of one positive Wassermann reaction two years ago. Frequent repetitions of the Wassermann, Kahn and Eagle tests yielded negative reactions. The patient has received dermatologic therapy with no change in the eruption. The stains made for fungi failed to reveal their presence.

Severe Stomatitis. Presented by DR. EDWARD A. OLIVER and (by invitation) DR. ARTHUR GREENBERG.

The patient, a salesman aged 56, noticed a grayish white patch on the undersurface of his lower lip during the latter part of May 1944. About a week later it spread to the lower part of his tongue. He consulted several dentists, without improvement. During the following five months his tongue became swollen and painful, and the lesions began to ulcerate. He received various forms of local therapy, together with arsenicals intravenously and a course of penicillin elsewhere, which have failed to alleviate the disease. Even though Vincent's infection is present, the cause of the basic lesion is unknown.

The examination reveals an ulcerative stomatitis involving the gums, tongue and mucous membranes adjacent to the teeth, especially the lower jaw. The membrane is excoriated, ulcerated, tender and painful and is covered with an easily removable foul exudate. The tongue is swollen and painful on movement.

The patient has had no elevation of temperature. The Wassermann and Kahn reactions were negative. The blood count was normal and no eosinophils were present. The smears showed spirilla, fusiform bacilli and gram-negative bacilli. The cultures yielded anaerobic long-chained streptococci. No fungi were found.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: This eruption is probably early pemphigus —that is, the initial lesion of pemphigus, which is often an oral lesion. I think that it may be a pemphigus localized in the mouth and that it may remain localized for a long time.

DR. EDWARD A. OIVER: We have watched this patient carefully for the past several weeks. The disease began last May. One thing against the diagnosis of pemphigus was the extreme pain he had suffered; it had been a most painful mouth. The only preparation giving any relief was an iodized phenol mouth wash. Gentian violet medicinal had no effect on the lesions. I believe, as Dr. Oppenheim and Dr. Nomland do, that this may turn out to be pemphigus.

DR. OTTO H. FOERSTER, Milwaukee: The thorough application of dry arsphenamine in powder form to the gums and tonsillar fossae rapidly heals Vincent's infections of the mouth, and I suggest its use here.

DR. E. P. LIEBERTHAL: I remember 2 cases of this type that Dr. Waldron, of Minneapolis, presented in 1920. He used dilute solution of sodium hypochlorite and removed the infected teeth. He made the point that the solution of sodium hypochlorite was superior to anything he had used previously.

Epithelioma of Finger (from Trauma?). Presented by DR. CLEVELAND WHITE.

I. F., a machinist aged 63, presents a growth at the base of the right index finger at the site of an injury due to a hot steel chip incurred two months ago.

According to his history, which has been checked, the injury was treated by his own physician, who noted no growth at the time, and no foreign body was found on roentgenographic examination. The wound healed. He was not seen by his physician for several weeks, but according to the history the growth appeared after the wound had healed.

The examination at the present time reveals a nodule the size of a hazelnut at the site of the original injury. There is a pearly border and a central depression.

On examination the blood and urine were normal. The Wasserman reaction of the blood was negative. A biopsy has not been performed.

DISCUSSION

DR. JOHN F. MADDEN, St. Paul: I do not think that a diagnosis can be made without a biopsy. Although the lesion looks more like an epithelioma than anything else, it may not be one.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I thought that clinically the lesion was a typical squamous cell epithelioma and should be excised widely. There is no need for a preliminary specimen for biopsy in a frank case of this kind.

DR. S. W. BECKER: For years I have been performing biopsies on small lesions. This lesion has the semiglobular shape of an early squamous cell epithelioma. This man is a machinist and insists that he hurt the finger. No one could work in a machine shop without knocking his knuckles; hence he has surely had multiple traumas. On the other hand, I have had women and men with such lesions on the face, where there has been no trauma. I do not believe that trauma can be called the chief factor in the production of this lesion.

DR. FRANCIS W. LYNCH, St. Paul: The question of the relation between trauma and cancer is one that deserves special consideration by those who are called before industrial commissions and the courts. There is an interesting and thorough discussion of the problem by Berenblum, a member of the Oxford Commission on Cancer (*Arch. Path.* **38**:233 [Oct.] 1944). It is an excellent discussion, which should be read by all who are interested in the problem.

DR. MAURICE OPPENHEIM (by invitation): I think that this is a case in which the diagnosis can be made only by biopsy. As Dr. Becker said, the lesion looks like cancer. It came on two months after injury. It is exceptional that a traumatic cancer originates from a normal skin. In most cases the real traumatic cancer develops on a base of a scar or on skin changed otherwise.

DR. S. W. BECKER: I have been astounded at the rapidity of growth in many of these tumors. I have one man who has been working with oil whom I have been treating for two or three years. Five or six of these growths have developed on the face and neck. He comes in with a typical squamous cell tumor, with a history that it has been present only two or three weeks.

DR. CLEVELAND WHITE: The interesting feature was the history of trauma. Of course, an absolute diagnosis cannot be made without a biopsy, but I feel as Dr. Montgomery does that it is a squamous cell epithelioma.

At the meeting last month Dr. Weber discussed the question of cancer due to trauma. Such cases are being encountered more frequently, and it has come to the point where one must try to determine whether or not trauma can clinically cause cancer. In the past three years I have seen a few cases of epithelioma in which trauma has allegedly been a factor. The physician who cared for this man at the time of the injury said that the wound healed rapidly and completely and that there was no sign of a growth until several weeks later. As Dr. Becker said, epithelioma can develop in a short time. As far as oil is concerned, I do not believe that a diagnosis of cancer due to oil can be made, because there is no folliculitis or comedos of any type. It is planned to have the lesion excised completely.

NOTE.—The tumor was excised completely by a surgeon and reported by the pathologist to be a grade I squamous cell epithelioma, with portions resembling pseudoepitheliomatous proliferation.

DR. STEPHAN EPSTEIN, Marshfield, Wis.: I agree with Dr. Becker and Dr. White that this is a typical squamous cell epithelioma. Ewing listed six essential criteria in determining the probable relation of trauma to tumors: (1) the authenticity and adequacy of the trauma; (2) the previous integrity of the wounded part; (3) a reasonable time relation, from three weeks to three years or more in certain cases; (4) continuity of symptoms of the injury with those of the tumor; (5) microscopic or other proof of existence and histologic type of a tumor, and (6) the location of the tumor at the point of injury.

The problem of trauma and cancer has interested me for a number of years. I have seen a fairly large number of cancers of the skin. One gets a history of trauma not infrequently—usually minor everyday traumas that do not appear significant. I found, however, that in those rare instances in which cancer of the skin originates before the age of 30, histories of definite well attested injuries are frequently volunteered. From these observations I am convinced that a single trauma can produce cancer.

Giant Nevus Pigmentosus and Verrucosus of the Thigh Treated by Complete Excision and Primary Grafting. Presented by DR. S. J. ZAKON and (by invitation) DR. J. T. GAULT.

A. G., a white man aged 40, was first seen on July 6, 1944. The examination revealed the presence of a pigmented verrucous hairy nevus, dark brown to black, involving the inner aspect of the left thigh and leg extending from the upper half of the thigh to the upper third of the leg. The nevus measured 12 inches (30 cm.) in length and 8 inches (20 cm.) in width and presented numerous fissures, most of which were secondarily infected and exuded a foul odor. At the bend of the knee there was a tender swollen eroded bleeding node. The patient's general condition was good. Biopsy of this painful lesion revealed an active melanotic nevus.

On July 28, after careful preoperative preparation, the entire nevus was excised with more than ¼ to ½ inch (0.64 to 1.27 cm.) margin of normal skin. The excision extended down to the subcutaneous tissues. The excised area was covered with sterile strips of petrolatum gauze, and a pressure bandage was applied. On August 18, a full thickness skin graft was cut from the donor areas with a Padgett dermatome. The sheets of skin were placed on the defect and were sutured to one another and to the periphery. The grafts healed by first intention, and the patient was sent home on September 10.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I believe that dermatologists have finally learned that this type of lesion should be treated by surgical excision first and not last. I think that it is a great mistake for any other type of treatment to be tried before excision is used. A certain percentage of these large nevi do become malignant, and removal is the best prophylaxis.

Favus in an American-Born Family. Presented by DR. MICHAEL H. EBERT.

R. P., a white boy aged 13, presents an eruption of the scalp, which he states has been present for two years. His sisters, aged 14 and 19, have the same eruption. They were all born and reared in Chicago. About 80 per cent of the scalp is involved, and the crown is almost bald. There are a few coin-sized irregular atrophic areas. The rest of the scalp is covered with a lemon yellow adherent crust with a mousy odor. There are many typical cup-shaped scutula. Typical hyphae were demonstrated in the scutulum.

DISCUSSION

DR. RUBEN NOMLAND, Iowa City: This is the third family I have seen in Chicago in which the third generation had favus.

DR. I. M. FELSHER: In the cases we had a few years ago there was a yellowish fluorescence under the Wood light.

Rhinosporidiosis. Presented by DR. OLIVER S. ORMSBY and (by invitation) DR. E. V. L. BROWN.

C. A. Mc., a single woman aged 56, was first seen by us, five weeks ago. There was a small tumor situated on the conjunctiva in the inner corner of the right eye, which had been present for six months. The lesion was the size of a small coffee bean and oval in contour. The color was purplish red, and the surface was covered with minute white spots. There were no subjective symptoms, but there was some increased lacrimation. One treatment with roentgen rays was given on the first examination, which had little effect on the tumor.

DISCUSSION

DR. OLIVER S. ORMSBY: I saw the patient several weeks ago, and I had no idea as to the diagnosis. I had not seen anything like it. As a therapeutic test we gave her one treatment with roentgen rays which reduced the tumor somewhat. The book on clinical mycology prepared by Dr. Callaway and others, which we recently received, presented an illustration of an identical lesion which was recognized by Dr. Ebert (Conant, N. F., and others: Manual of Clinical Mycology, Prepared Under the Auspices of the Division of Medical Sciences of the National Research Council, Philadelphia, W. B. Saunders Company, 1944, p. 200). The examination for the spores has to be done as one would examine for other spores, with potassium hydroxide. The organisms cannot be grown; hence nothing can be proved by bacteriologic examination. I take it that examination of the material in these lesions is not hard to demonstrate. We are going to demonstrate the spores as soon as possible.

This disease occurs in the tropics, and some of the lesions are extensive and in some areas become large masses. In some cases the disease is serious. The cases in which the eyes are involved are classic. The description of these cases as given in the aforementioned book is exactly as seen here—a small nodule or tumor, bluish red, with white bodies on its surface. It is the white bodies that contain the material in which the micro-organisms are found.

Rosacea-Like Tuberculid of Lewandowski. Presented by DR. S. ROTHMAN and (by invitation) DR. A. I. SHAPIRO.

I. O., a white woman aged 32, was first treated in the University of Chicago Clinics in 1936, for acne vulgaris. After a lapse of three years she returned, in 1939, with a facial eruption which was diagnosed clinically and histologically as rosacea-like tuberculid of Lewandowski. For the next nine months she was treated with local ultraviolet irradiations given with the water-cooled quartz mercury vapor arc lamp, and she received twenty intravenous injections of gold ammonium succinimidate in graduated doses of from 25 to 500 mg., with some improvement.

In August 1944, the patient again returned, because of an exacerbation of the eruption. She presented small red papules spread densely over both cheeks and forehead. On diascopic pressure yellowish brown spots remained at the site of the papules. The nose, perioral region, center of the chin and side surfaces of the forehead were completely free. Treatment similar to that which she received four years previously was instituted, and decided improvement has been noted.

A biopsy section is presented. It shows a massive infiltrate, consisting of round cells, epithelioid cells and giant cells, extending rather deeply into the corium.

Roentgenograms of the chest have consistently revealed normal pulmonary fields and heart. Tuberculous foci have never been found. Old tuberculin in a 1:10,000 dilution elicited a negative reaction and in a 1:1,000 dilution a positive reaction. The Wassermann and Kahn reactions of the blood were negative. The blood count was normal, except for a transitory leukopenia during the course of the injections of the gold preparation.

The patient has been pregnant three times. The first pregnancy resulted in an anencephalic stillborn baby; the second terminated in the birth of a 6 month

premature baby which died; the third resulted in a normal baby, delivered by cesarean section because of a placenta previa.

DISCUSSION

DR. H. E. MICHELSON, Minneapolis: I wish I were able to crystallize an opinion on this condition, but all I can do is to give you my convictions in the matter. Dr. Laymon and I prefer the name "maculopapular tuberculid" in preference to "rosacea-like tuberculid." We have voiced our objections to the latter term before. We think that the clinical criteria are that the papules are small, are not necrotic, have a dark red color and do not coalesce and that the microscopic observations closely simulate those found in sarcoid. In our experience the course is extremely variable. Some patients get well without treatment in a short time; others do not respond to any treatment, but later the lesions do disappear. Some of the patients react positively to tuberculin, and some do not. Unfortunately, the bacilli cannot be found, although the presence of tuberculosis has been demonstrated in a fairly large percentage of the patients. Dr. Miescher not long ago reviewed a series of these cases, and he felt that in frank rosacea there was a similar microscopic picture at times. This we have been unable to corroborate. I believe that there are some papular rosaceas that look just like this eruption but are not tuberculous, and I do not believe that when an antirosacea regimen does not bring about a cure the disease is therefore tuberculosis. We are convinced that the diagnosis of rosacea-like tuberculid is made much too often.

DR. HAMILTON MONTGOMERY, Rochester, Minn.: The histologic sections in this case show typical tubercles and not just a few collections of epithelioid cells. I agree with Dr. Michelson that one sees collections of epithelioid cells in cases of diseases that have been diagnosed as various forms of tuberculids but which more probably were rosacea not tuberculids. In the present case, however, the histologic structure is definitely that of tuberculosis.

DR. OLIVER S. ORMSBY: I should like to make a therapeutic suggestion, which I rather dislike to do in view of the fact that treatment is considered ineffectual by many. I have shown to this society a patient with generalized sarcoid that was cleared with ethyl chaulmoograte. Because of the good results secured also in 2 cases of rosacea-like tuberculid, I suggest its use for patients that have resisted other methods of treatment.

DR. C. W. LAYMON, Minneapolis, Minn.: I merely want to say a word about sensitivity to tuberculin in these cases. Some observers have stressed the importance of a high degree of sensitivity in this type of tuberculid in contrast to a much lower degree of sensitivity in tuberculosis miliaris disseminata, for example. In the cases of so-called rosacea-like tuberculid which we have studied at the University of Minnesota there has been such a tremendous variation in the reactions to tuberculin that it has been of little importance diagnostically.

DR. S. ROTHMAN: I am grateful for Dr. Ormsby's therapeutic suggestion and will gladly follow it.

I agree with Dr. Michelson that "rosacea-like" is not a fortunate adjective. But I object even more to the term "tuberculid." In modern dermatology I believe that the term "tuberculid" should be restricted to eruptions which are due to a shower of tubercle bacilli embolizing in the skin in persons with an extremely high degree of tuberculous allergy. Owing to this allergy the embolizing tubercle bacilli are more or less rapidly and more or less completely destroyed in the skin. Therefore, animal inoculation and histologic demonstration of bacilli in lesions of tuberculids is rarely successful, and histologically one finds all transitions between banal inflammatory infiltrates and classic tuberculous structure, obviously dependent on the speed with which tubercle bacilli are decomposed. According to this definition three diseases can be called tuberculids: lichen scrofulosus, papulonecrotic tuberculid, including the follicular-papular forms, and erythema induratum of Bazin. In all these diseases one finds strong reactions to tuberculin in dilutions

of 1 : 1,000,000 or at least 1 : 100,000, and one can safely assume that the patient harbors living tubercle bacilli somewhere in his body. This is not the case with sarcoidosis, tuberculosis miliaris disseminata faciei and Lewandowski's disease. The last two diseases display tuberculous or tuberculoid structure histologically, but there is no definite evidence that they are due to tuberculosis. If they are, it must be the local action of a greatly mitigated bacillus, because the clinical course is torpid, tuberculosis is never found in internal organs and the sensitivity to tuberculin is of a conspicuously low degree—in any case never as high as in tuberculids. This patient's reaction to tuberculin, for instance, is negative to old tuberculin in a dilution of 1 : 10,000 and only weakly positive to old tuberculin in a dilution of 1 : 1,000; this is the average reaction of a city dweller. The clinical significance of a sharp separation of these diseases from "tuberculids" is obvious. In tuberculids one has to search for active tuberculous lesions, because the presence of tuberculids means activity, whereas tuberculosis miliaris disseminata faciei and Lewandowski's disease do not mean that. Therefore, I am sorry that I cannot agree with Dr. Laymon. I believe that the thorough quantitative study of sensitivity to tuberculin in all these diseases contributes a great deal to one's understanding of the pathogenesis of cutaneous tuberculosis and is clinically highly important.

A Case for Diagnosis (Periarteritis Nodosa?). Presented (by invitation) by Capt. Lester W. Kimberly, M.C., A.U.S.

M. J. S., a white man aged 25, first noticed small tender nonpainful nodules on the flexor surface of the right forearm in October 1942. About seven months later he noted similar nodules on the left side of the abdomen and also that the nodules on the right forearm were disappearing leaving a mottled reticulated bluish network outlining the pattern of the blood vessels in the skin or subcutaneous tissue. Since then new nodules have continued to appear about the waist, on the lower part of the abdomen, in the crural area, on the thighs, in the right popliteal space and on the chest, back, arms, forearms, palms and soles. They vary from a few millimeters to 1.5 cm. in diameter, and are firm, discrete and movable. Most of them have receded, leaving the reticulated pattern now seen.

The Kahn reaction of the blood was negative, as was that of the spinal fluid. The urine and blood were normal. The results of gastric analysis were within normal limits. The sedimentation rate was 10 mm. in one hour. The values for blood chemistry were within normal limits. The roentgenograms of both legs and both forearms revealed no changes of soft tissues or bones; those of the heart and lungs showed no abnormalities.

Histologic examination of a late lesion showed no essential change in the epithelial hair, sebaceous glands and sweat glands. At the junction of the dermis with the subcutaneous tissue there was an area of chronic inflammatory reaction characterized by an infiltration of lymphocytes, plasma cells, eosinophils and macrophages and some areas containing polymorphonuclear leukocytes. The infiltration of inflammatory cells involved the fibrous tissue. The perivascular spaces were also involved; these were more striking at the margins of the lesions. The inflammatory cells were primarily of the mononuclear type previously mentioned. There was a thickening and increased cellularity of the smaller vessels, many appearing to be almost solid cords. The adventitia about some of the larger vessels was edematous, containing chiefly lymphocytes and plasma cells. Occasionally there were a few inflammatory cells within the larger arterial walls. The histologic changes of the lesion were considered nonspecific.

DISCUSSION

Dr. C. W. Laymon, Minneapolis: This to me was one of the most interesting cases of the day. In most cases, unfortunately, the diagnosis is made post mortem by the pathologist. The mortality is high, and males are affected much more frequently than females. The kidney, heart and liver are involved much oftener

than the skin. Reddish or purplish brown reticular lesions such as were seen in this case are suggestive of a relatively benign or chronic type of periarteritis nodosa.

DR. RUBEN NOMLAND, Iowa City: The experience at the University of Iowa is that the cases of periarteritis nodosa that come to necropsy have mostly been from the neurologic service, because the patients had had neurologic symptoms as their chief complaint. One of the conditions that the pathologist at the University Hospital has been able to demonstrate is an involvement of the peripheral nerves. The sections show a chronic inflammation about a medium-sized nerve.

DR. MAURICE OPPENHEIM (by invitation): The nodules in this case looked like those of periarteritis nodosa. There are definite infiltration and nodulation. In my department of dermatology in Vienna I gave such a case the name of "apoplexia cutanea," because a sudden deep hemorrhage of the skin originated. The patient, a woman, died suddenly during my rounds, and histologic examination showed periarteritis nodosa of the skin and of the internal organs. With regard to the skin the foci were located around the bifurcation of the arteries in the subcutaneous tissue. The case was published by my assistant Dr. Freund in the German *Archiv für Dermatologie und Syphilis.* I believe, as does Dr. Laymon, that this is one of the exceptionally rare cases of periarteritis nodosa of the skin.

DR. ARTHUR C. CURTIS, Ann Arbor, Mich. (by invitation): I was glad to see this case for two reasons. I have seen several cases of periarteritis nodosa that have been diagnosed ante mortem, but this is the first case in which there has been an erythematous eruption or, for that matter, an eruption of any type. Second, the patients I have seen have not had the characteristic nodules along the vessels. One would think that this would be a common finding, but too often many patients are seen before nodulation occurs. The pathologists see nodules often; the clinicians, seldom. This patient has the most striking nodules along the brachial artery that I have ever seen.

Periarteritis nodosa is a disease that has several stages. It often begins like an infection, and frequently bronchial asthma, urticaria or erythema multiforme is present. In the acute stage, a high fever, leukocytosis and eosinophilia with a count of 30, 40 or 70 per cent may be present. As the disease progresses, and if the patient does not die, a chronic state is reached, which is represented by this patient. The leukocyte count is normal, and the eosinophils have fallen to a normal of 2 per cent. He has no manifestations of activity of his disease, except fatigue and a history of loss of weight.

Dr. Rich, at St. Louis, has produced in animals a pathologic picture identical with periarteritis nodosa by inducing in them sensitivity to injected horse serum and then giving large doses of this protein parenterally.

DR. PAUL O'LEARY, Rochester, Minn.: My concept of periarteritis nodosa is similar to that of Dr. Nomland in that sensory changes in the skin are commoner than are the dermatologic ones. In fact, the cutaneous picture is so varied that it has been quite impossible up to date to describe the classic cutaneous picture of this syndrome.

Several years ago a patient with anesthetic areas about the face, especially about the mouth, and about the arms and chest, with associated pigmentary changes in these areas, was found to have acid-fast bacilli in the smear of nasal material. These organisms were similar to Hansen's bacilli and were accepted as such by the laboratory at Carville, La. The patient died shortly thereafter, after an acute flare-up of a previously recognized nephritis, and at autopsy a diagnosis of periarteritis nodosa was made and no evidence of leprosy was demonstrated.

I have had a similar experience in which acid-fast organisms were demonstrated in a similar case, and, while I do not for a moment infer that this patient has leprosy, I hope that Captain Kimberly will have the opportunity to examine a smear of nasal material for acid-fast organisms.

DR. S. W. BECKER: I was much impressed by the vascular changes. I thought of livedo racemosa of Ehrmann. I stroked the skin in order to express the blood from these areas, and the blood returned somewhat slowly, but it returned as

venous blood, which identifies the disease as an obliterative one. Ehrmann's patients usually had tuberculosis or syphilis. This man's disease is evidently a more acute affair, but the vascular change is evidently similar to, if not the same as, that in Ehrmann's livedo racemosa.

CAPT. LESTER W. KIMBERLY, M.C., A.U.S. (by invitation): I presented this case in the hope that I might get some therapeutic suggestions. I had never seen anything like it before.

NOTE.—The patient was subsequently given 1,200,000 units of penicillin, without any effect on the development of new lesions.

Idiopathic Multiple Pigmented Sarcoma (Kaposi?). Presented (by invitation) by DR. MAURICE OPPENHEIM.

L. O., a white man aged 42, presents on both soles, on the lateral parts of both feet and over the ankles symmetric bluish red spots and infiltrated plaques with a smooth surface. The macules vary in size from that of an almond to almost diffuse involvement of the soles. The margins are sharp. Diascopy revealed a yellow-brown color. There are no erosions or ulcerations. On several toes of the left foot there are pinhead-sized nodules, sharply limited, of dark blue color and hard consistency, like warts. On both legs there are sharply limited round depressed pigmented scars the size of a dime.

The disease began seven years ago in Italy without subjective symptoms. The patient has diabetes, but the urine is now free of sugar, and the blood sugar level is 130 mg. per hundred cubic centimeters. He is on a diet for diabetic patients. He was never treated by a dermatologist. He is now taking solution of potassium arsenite, U.S.P., and grenz rays are to be used.

The urine was normal except for a faint trace of acetone. The blood count was normal. The differential count showed 4 per cent eosinophils. The blood cholesterol level was 143 mg. per hundred cubic centimeters.

A section from a diffusely infiltrated area of the ankle was removed for histologic study, with the following results: The epidermis was normal; the papillary layer was partially flattened. There were many newly formed capillaries, partially enlarged and partially closed by a growth of endothelial cells. At some places there were formations resembling angiomas. There was necrosis of the connective tissue in the neighborhood of the capillaries. Lymphocytic elements and a few mast cells and plasma cells were present. There were many enlarged lymphatic vessels. There were no hemorrhages, but hemosiderin, mostly extracellular, was present in all parts of the tissue. The connective tissue was acidophilic and poor in fibrocytes. In some areas the sweat glands were cystic and hypertrophic.

DISCUSSION

DR. HAMILTON MONTGOMERY, Rochester, Minn.: I believe that this is a case of Kaposi's sarcoma. The histologic changes are not so typical as one usually sees. There are no sarcomatous changes or collections of lymphocytoid cells. There is proliferation of the walls of the capillaries, resembling in some respects the early phases of hemangioendothelioma. Some French authors regard Kaposi's sarcoma as a hemangioendothelioma. The sections also show definite disposition of pigment, and if stains for iron were made would, I believe, reveal the pigment to be hemosiderin and not melanin. The histologic picture in this case would explain and fit in with the long duration of the process.

DR. DAVID LIEBERTHAL: The most interesting point in this case is that the disease remained stationary for years without the patient's having received any treatment during the time. In this disease one sees progressive development in the spread and the clinical changes and after a few years a fatal termination.

DR. MAURICE OPPENHEIM (by invitation): Clinically, there is no doubt that it is Kaposi's sarcoma. The infiltration, the purplish color, the location of the pigmented scars on the legs, the symmetry and other aspects are typical. As Dr.

Lieberthal says, it shows a chronic course. Such cases are known to occur. But more interesting are the histologic observations. As I saw the histologic structure, I thought first of hemangioendothelioma tuberosum multiplex because there are many newly formed capillaries, sharply limited against the enlarged tissue. There are many enlarged lymphatic vessels, and the connective tissue is almost unchanged. It looks like the third stage, the so-called angiomatous stage, of the disease. There were no spindle cells in the tissue. This is remarkable in a case of pigmented sarcoma of Kaposi, especially in such a chronic case. All through the section hemosiderin was present in large amount; hence there is no doubt that many hemorrhages took place.

As Dr. Lieberthal says, this case should be studied. There was only 130 mg. of sugar per hundred cubic centimeters of blood. It is possible that this disease has something to do with the diabetes, but the cholesterol level is only 143 mg. per hundred cubic centimeters; hence I am a little doubtful that the case should be diagnosed as a true case of Kaposi's sarcoma. Clinically it is, but histologically it is not so certain.

Dr. Hamilton Montgomery, Rochester, Minn.: There are cases of Kaposi's sarcoma described in the literature with histopathologic changes similar to those seen in this case.

Dr. Maurice Oppenheim (by invitation): In Gans's "Histology of Skin Diseases" there is a picture of Kaposi's sarcoma which is similar to the histopathologic changes in my case. Ordinarily one would hesitate a little to consider these cases as instances of Kaposi's sarcoma.

Pemphigus Erythematosus(?). Presented by Dr. Herbert Rattner and Dr. Theodore Cornbleet and (by invitation) Dr. M. S. Kagen.

A 63 year old white man of Polish extraction had thick greasy scales on the scalp at the age of 40. Seven weeks ago yellowish scales appeared on the alae of the nose, followed by blisters on the hands, chest, back, face, legs and forearms. The patient has improved with treatment consisting of potassium permanganate baths, 1 per cent gentian violet medicinal, dusting powders, 40 per cent sulfur paste and acetarsone and sulfadiazine administered orally.

DISCUSSION

Dr. Francis E. Senear: I felt that this was not pemphigus erythematosus but rather a true pemphigus vulgaris. The lesions on the scalp have been present for some time and may be looked on as the primary lesions which Dr. Oppenheim has written about and talked about. The generalized eruption is of only seven weeks' duration. I have seen 2 cases of pemphigus erythematosus in which that typical picture had existed for some time, and subsequently there developed a bullous eruption typical of pemphigus vulgaris. I have never seen that happen with the rapidity that has taken place in this case, however. Furthermore, the lesions on the alae nasi seem to be vegetative ones, such as are seen in pemphigus, but not the lupus-erythematosus-like lesion seen in the more benign type of the disease.

Dr. Theodore Cornbleet: I naturally had in mind the various members of the bullous group, particularly erythema multiforme and pemphigus. The exact placement in the pemphigus group, if this is pemphigus, we were not certain about, but the rapidity and the greatness of the changes that can occur in the eruption in the erythematous type of pemphigus should make one think of this as a label for this patient's disorder. This may be the correct diagnosis, but a definite one had perhaps better wait for the future.

Adiponecrosis Subcutanea Neonatorum. Presented by Dr. David V. Omens and (by invitation) Dr. Harold D. Omens and Dr. M. S. Kagen.

W. G., a Negro boy aged 5 weeks, presents a hardness of the skin of the back involving almost the entire back and extremities, especially the lateral aspects.

This hardness appeared three days after birth in localized areas which spread and coalesced to the present involvement.

On Dec. 10, 1944, the mother, a 28 year old Negro woman, was brought into the hospital in the early part of the last month of her pregnancy, with a temperature of 103 F. It was decided to induce labor, which was done by rupturing the membranes. The labor was short and not difficult, the baby being born with head presentation. During labor the mother was given sedatives (Stroganoff's method). On delivery the child was cyanotic and subsequently showed repeated manifestations of cyanosis with conjunctival hemorrhages. Because its condition gradually became worse, on the third day the child was removed to the Children's Hospital, where the cutaneous manifestations began to appear and were accompanied with a fluctuating temperature ranging from 100 to 103 F., with abscesses which on culture showed Staphylococcus aureus. Culture of the blood yielded the same organism. The Kahn reaction of the mother's blood was negative. The child has been given sulfonamide compounds, and for the past three days the temperature has been normal and he is showing improvement in health.

The histologic examination of a specimen removed showed a mild acanthosis of the epithelium, edema of the collagenous tissue of the entire cutis, dilatation of the lymph and blood vessels and an increase in the connective tissue cells. The appendages of the skin participated in the edematous process. In the junction of the cutis and the subcutaneous fat there was an infiltrate composed of small lymphocytes, plasma cells, histiocytes and fibrocytes which tended to involve the trabeculae of the fat cells, which were thickened and contained a homogeneous substance like a coagulum.

DISCUSSION

DR. C. W. LAYMON, Minneapolis: A diagnosis of necrosis of subcutaneous fat should be strongly considered in this case. The disease appears from a few days to three weeks after birth and disappears spontaneously within a few months. The locations of the lesions in this case were characteristic, being on the back, buttocks and extremities. True sclerema neonatorum occurs within the first few days of life in debilitated babies and is almost always fatal within a short time. The involved skin is firm and shrunken and cannot be lifted in folds as in this case.

DR. S. ROTHMAN: Sclerema neonatorum represents a diffuse solidification of the subcutaneous fat tissue due to a pathologic shift in the composition of the fat. The body temperature is subnormal, and the babies die in a few days. The circumscribed hard cutaneous-subcutaneous nodes with slight erythema on the surface in the presented case correspond with what was described as adiponecrosis subcutanea neonatorum. It is probably due to injuries received during delivery, and its prognosis is absolutely favorable.

DR. DAVID V. OMENS: In answer to Dr. Laymon, I would say that the area he felt was the uninvolved area. In the areas that were definitely involved he would have found it difficult to raise the skin from the underlying tissues. There was a grayish color to the cut surface of the subcutaneous tissue. The patient has what I thought were the characteristic features that were primarily described by Dr. Gray, of London, England, twenty years ago.

The histologic section presented what looked like a coagulum of the fatty tissue. The fat cells were filled with a protoplasmic substance which took origin from the fat cell membrane or trabeculae, with a lymphocytic cellular infiltrate above the surface of the fatty tissue extending down to involve the trabeculae, and there was no evidence of necrosis in the entire section.

Seborrheic Dermatitis with a Decided Palpebral Involvement. Presented by DR. MICHAEL H. EBERT.

P. B., a white man aged 28, presents a decided inflammation on the margins of the eyelids and an eruption in the bearded region. He states that the lids have been involved since he was 2 years old and that he has had many types of treatment in hospitals for diseases of the eye, including surgical removal of the margins

of the lower lids. In May 1943, redness and scaling appeared in the bearded region, which were cleared in 1944 by roentgen ray therapy. After three months the eruption recurred and persisted. There is ectropion of the lower lids, with an operative scar along the palpebral borders. The palpebral conjunctiva is granulomatous. There is a mild blepharitis of the upper lids. The bearded region is dull, red and scaly.

DISCUSSION

DR. THEODORE CORNBLEET: May I suggest the possibility of sycosis barbae for consideration? The eyelashes are involved, something that I have seen happen before in this disease.

DR. MICHAEL H. EBERT: Dr. Cornbleet's point is well taken. When we saw this man for the first time, on January 8, he was in rather poor condition: He had a long beard; his hair was shaggy, and he was dirty. When the beard was clipped the eruption appeared. When I saw him again, there were a diffuse infiltration and redness but no pustules. Yesterday there were no pustules, but today there are definite follicular pustules. I accept the diagnosis of sycosis barbae with secondary dermatitis of the bearded region and involvement of the eyelashes. The extraordinary thing in this case is the early onset. I think that the involvement of the lashes is due to the same type of staphylococcus that lives on the skin.

Ainhum. Presented by DR. DAVID V. OMENS and (by invitation) by DR. HAROLD D. OMENS and DR. M. S. KAGEN.

L. S., a Negro butcher aged 39, complains of pain in the small toe of the left foot which is severe on excessive walking and at night when resting.

On examination there is a constricting ring just below the first phalanx encircling the entire toe and producing a bulbous distention of the distal portion of the toe. A roentgenogram revealed no osseous involvement but just a constricting ring of the soft tissues. The report on the Wassermann test has not been returned.

This patient has lived in Chicago for the past twenty-seven years; previous to that time he lived in New Orleans. He said that he has not walked barefooted and has had no injury to his feet at any time; however, he stated that on that particular toe he had a corn which is not present now.

DISCUSSION

There was no discussion of this case.

A Case for Diagnosis (Squamous Cell Epithelioma?). Presented by DR. MICHAEL H. EBERT and (by invitation) DR. M. S. KAGEN.

M. G., a Negro woman aged 25, presents an ulcerated area, 5 cm. in diameter, to the left of the anus. A "boil" appeared in this area eleven months ago, and a similar one appeared on the opposing surface of the right nates. The one on the right disappeared in a few weeks, but the one on the left persisted and ulcerated. The ulcer was so tender it interfered with walking. She has congenital syphilis and had intermittent treatment until 1941. The Wassermann reaction of the blood serum is positive at the present time. The Frei test elicited a negative reaction. Since the patient received a course of sulfathiazole the ulcer has cleared and is much less tender. At present there is an irregularly outlined ulcer 5 cm. in diameter. The floor is granulomatous, with a few persistent islands of epidermis. The border is level with the surrounding skin and not undermined. The base is moderately infiltrated.

DISCUSSION

DR. LOUIS H. WINER, Minneapolis: The histologic section was spread all over the slide. I showed it to Dr. S. W. Becker, and he agreed with me that there was an island which showed epidermal proliferation much in the manner of a squamous cell epithelioma; hence, I offer that as a diagnosis.

DR. MICHAEL H. EBERT: The section was taken from the inner margin near the active ulcer, but the tissue was so friable that the pathologist could do no

better with the slide. I thought that there was more epithelial proliferation than one sees in pseudocarcinomatous changes in marginal ulcers, and from the histologic appearance I was almost inclined to think that it was an epithelioma.

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Jan. 19, 1945

A Case for Diagnosis. Presented by DR. THOMAS BUTTERWORTH, Reading, Pa.

T. S. R., a white man aged 35, a robust steel worker, presents a raised, annular, circinate, serpiginous and flesh-colored eruption involving the back and posterolateral aspects of the neck. The eruption had its onset about Nov. 1, 1943; it has improved at times but never entirely healed.

The serologic tests of the blood for syphilis elicited were negative reactions. The urine was normal. The biopsy specimen was reported as characteristic of atypical lupus erythematosus, conceivably with a tuberculous base.

The patient was given 900 r of roentgen rays in divided doses to selected lesions, without effect. Bismuth subsalicylate in oil, 1.25 cc. of a 13 per cent suspension, was administered weekly for eight weeks. Various keratolytic ointments were without value.

DISCUSSION

DR. SIGMUND S. GREENBAUM: The histologist did not make a diagnosis; hence at least the provisional diagnosis will have to be made clinically, which happens not infrequently.

DR. MORRIS MARKOWITZ: Histologic examination shows a few things—for instance, numerous fibroblasts and basophilic degeneration—which occur frequently in granuloma annulare. However, it could also be a tuberculous disease.

DR. SIGMUND S. GREENBAUM: I do not think that it is lupus erythematosus clinically. I think that it is closer to granuloma annulare or to a type of serpiginous sarcoid than it is to anything else. It would be interesting to see the effects of irradiation on one of those annular lesions on the left side of the neck and of arsenic taken by mouth. This patient should be presented again in thirty or sixty days.

DR. MORRIS MARKOWITZ: Why not destroy one half or one third of the lesion by electrocoagulation? It sometimes happens that when one lesion is destroyed by electrocoagulation the others disappear spontaneously.

DR. HERMAN BEERMAN: This histologic section is so well made and so clear that all the features which Dr. Weidman has on his protocol are easily observed independently by any one looking at it. I cannot see anything there to suggest granuloma annulare. In fact, the striking thing is the fact that it looks more like lupus erythematosus, and then when one looks at it closely it does not. I think from reading Dr. Weidman's note that he had the same opinion.

DR. MORRIS MARKOWITZ: Basophilic degeneration and fibroblasts occur in granuloma annulare.

DR. HERMAN BEERMAN: Basophilic degeneration is seen in warts, too.

DR. JOHN F. WILSON: Has the eruption always looked the same?

DR. THOMAS BUTTERWORTH, Reading, Pa.: Approximately the same. At times it gets better and then reverts to the form seen tonight. I do not want to electrodesiccate any of the lesions, because they disappear without any scarring. I do not want to do anything poorer than Nature is doing.

DR. CARMEN C. THOMAS: Have you tried to exclude light from the lesions?

DR. THOMAS BUTTERWORTH, Reading, Pa.: On what grounds?

DR. CARMEN C. THOMAS: On general principles. I do not know the nature of the patient's work. Is he exposed to arc lights?

DR. SIGMUND S. GREENBAUM: Each of those lesions has an unusual filiform infiltrated border, and Dr. Corson presented a case like this years ago, which was pictured in the textbooks as a circinoid type of sarcoid. If the histologic conditions definitely exclude granuloma annulare, I think this is the only other condition to think of, clinically.

DR. HERMAN BEERMAN: It does not look like that, either, histologically.

DR. SIGMUND S. GREENBAUM: Well, a good many of the histologic diagnoses do not agree with what one sees clinically. Many times one cannot make the diagnosis on histologic grounds.

DR. MEYER L. NIEDELMAN: Was the biopsy specimen taken from one of the older lesions?

DR. THOMAS BUTTERWORTH, Reading Pa.: One cannot say that one lesion is older or younger. The whole process is in a state of flux.

DR. SIGMUND S. GREENBAUM: I would use solution of potassium arsenite U. S. P. Kissmayer thinks that all lesions clear up with arsenic.

Familial Lentigines. Presented by DR. MORRIS MARKOWITZ.

The McC. family presents a family group of three brothers and three sisters and a father. The mother, who is dark-haired, is not affected. The patients are red-headed, except for a dark-haired 9 year old boy and a blond 19 year old girl. The ages of the children range from 7 to 19 years. The lesions had been noticed soon after birth, and their characteristics remained unchanged in all seasons (they are not affected by sunlight). They are symmetrically located on the face, shoulders and upper part of the back, appearing as round noncoalescent macules, of a yellow color and ranging from a pinhead to a pea in size.

Determinations of the blood chemistry of the 2 boys, aged 7 to 9 years, showed: cholesterol, 200 to 220 mg.; calcium, 10 to 15 mg.; sugar, 100 to 120 mg., and urea nitrogen, 9 to 20 mg., per hundred cubic centimeters of blood.

DISCUSSION

DR. THOMAS BUTTERWORTH, Reading, Pa.: I think that is the common combination in the Irish—red hair and freckles.

DR. MORRIS MARKOWITZ: Should one call that simply freckles, or should one make a distinction between freckles and lentigines? I think that I should make a distinction.

DR. SIGMUND S. GREENBAUM: Of course the French and, I think, the Germans differentiate lentigines and freckles. These patients have freckles. The boys have them on the face and on the shoulders. Sometimes the differentiation between lentigines and freckles is not easy. I saw a patient only today with hundreds of pigmented lesions on the shoulders and face, developing after exposure to sunlight. While it is often difficult to differentiate lentigines and freckles, I think that in this case it can be done. Lentigines, by the French and, I think, by Ormsby, are placed in the group of pigmented nevi developing late in life and sometimes under the influence of chemical rays or sunlight or roentgen rays. These patients have freckles, not lentigines.

DR. MORRIS MARKOWITZ: Another thing one would not think of with regard to freckles is that they are not changed by exposure to light but sometimes become more prominent in the dark. These occurred soon after birth. Usually freckles appear when the child is 5 or 6 years old.

DR. JOHN F. WILSON: The shoulder strap regions are less involved, and the "V" of the neck is fairly sharply marginated.

DR. SIGMUND S. GREENBAUM: Yes, the sunlight brings the freckles out. I think that some one makes the distinction that the melanin is deep down in the basal cell layer in lentigo.

Nevus Pigmentosus Lateralis. Presented by DR. REUBEN FRIEDMAN.

K. F., a white boy aged 7 years, presents numerous areas of light brownish hyperpigmentation confined to the left side of the chest, the left arm and the left side of the back and neck. One brownish streak, about 0.5 to 1 cm. wide, extends from the middle of the extensor surface of the left forearm up along the inner aspect of the arm and across the left shoulder, terminating behind the acromion process. Two shorter linear parallel processes are noted on the posterior aspect of the left arm. A large irregular patch on the left side of the back extends upward along the vertebral column from the fifth lumbar vertebra, gradually fanning outward and upward and then curving across the upper part of the back to the neck and shoulder. Another patch is located on the chest, extending from the middle of the manubrium sterni to the shoulder. There have recently developed two small patches of faint hyperpigmentation in the right portion of the epigastric region and at the right costal margin.

The Wassermann reaction of the blood was negative.

Shortly after the patient's birth his mother noted a small, thin, linear area of hyperpigmentation about ¼ inch (0.64 cm.) long, on the middle of the outer side of the left arm. It remained stationary for a year and then began to spread from that point both upward and downward in linear fashion. New similar patches have developed from time to time.

DISCUSSION

DR. SIGMUND S. GREENBAUM: Another interesting thing about this case is that the youngster has three new café-au-lait pigmented spots developing on the chest, one anteriorly and two posteriorly. He is sure that they are new ones, and I agree with him. This eruption was small in the beginning but has increased from time to time. I think that one ought to consider not only a simple condition of unilateral pigmented nevus but the condition described by Block and Sulzberger. There is not an increase of melanin or an increased dopa reaction, but an absence of real nevic cells; hence a biopsy, if possible, might be of interest for a later report. It is not an out and out case of the reticulated pigmentary type which Bloch and Sulzberger have described, but this diagnosis has to be considered.

DR. REUBEN FRIEDMAN: Montgomery reviewed the subject of unilateral nevi in 1901 and found that this disease had been given some forty-eight different designations by that many different investigators, and each one had so qualified the appellation as to give some intimation of the causative factors involved according to the thought of that investigator. He mentions the fact that linear nevi often follow the course of cutaneous nerves and sometimes are found along Voigt's lines. I called the attention of some of our members tonight to the fact that the initial nevus on the arm follows the course of one of the superficial veins, and this also is mentioned by Montgomery as a possible causative factor—the lines following the distribution of cutaneous vessels. Some other investigators, I think, ascribe the disease to some disturbance in growth of embryonic tissue, and others state that linear nevi run in the metameres or segments of the body.

DR. SIGMUND S. GREENBAUM: Some of those occur with ectodermal defects. I could not see how in this case the lesions follow a nerve, unless it is the axillary nerve. And one cannot ignore the fact that new spots are coming out on this child.

DR. FRITZ CALLOMAN (by invitation): This demonstration of a unilateral nevus—showing a straight linear course in its brachial part and a metameral distribution in its scapular part—appears significant. Through decades the problem of the linear or metameral development of malformations and diseases of the

skin has been discussed and will continue to be studied. Linear development of moles usually is limited to the extremities. However, not infrequently this course has been observed also with moles of the body or face. Contrarily, diseases of the skin, such as neurodermatitis or scleroderma, when showing a linear development almost always have been observed on the skin of the upper or lower extremities, while their linear appearance on the body is extremely uncommon, and the diseases are not often found in the facial region.

The case directs attention to one of the old standard works of international dermatology which has not lost its significance up to the present time. I refer to A. Blaschko's memorable atlas published in 1902, under the auspices of the "Deutsche dermatologische Gesellschaft" (Die Nervenverteilung in der Haut in ihrer Beziehung zu den Erkrankungen der Haut, Vienna, W. Braumüller). In it the so-called "nevus-lines" have been systematically registered, tabulated and analyzed from material collected in an enormous number of reported cases.

As to the case under discussion, it is probable that an analogous observation may be found in Blaschko's atlas.

Erythema Annulare Centrifugum. Presented by DR. CARROLL S. WRIGHT and DR. E. R. GROSS.

R. B., a white man aged 60 years, presents, chiefly on the back, a number of asymmetric, annular, elevated, slightly reddened lesions, some of which are several inches in diameter. The lesions tonight have lost the annular appearance that they had when the patient was last seen, in December. For thirty years the patient has had an eruption, chiefly on the trunk and most pronounced on the back. This has been intermittently better and worse but has never disappeared. There are no local or constitutional symptoms.

DISCUSSION

DR. SIGMUND S. GREENBAUM: I saw this patient as a private patient about two years ago, and, just as tonight, he had a nodular eruption. The term "erythema annulare centrifugum" excludes a nodule. I told Dr. Wright that I did not think it was that; but there were lesions similar to erythema annulare centrifugum, and no doubt Dr. Wright saw the patient when he did have that type of lesion. But he does have nodules. I took a biopsy specimen and sent a section from one of the nodules to Dr. Weidman, and he made the provisional diagnosis —not clearcut—of mycosis fungoides, also mentioning aleukemic leukemia as a possibility. The blood picture, however, did not show anything of significance. He has no itching, and he has had the disease for thirty years; hence one would be inclined to exclude mycosis fungoides on that basis. I think that eventually, however, this will prove to be one of the lymphoblastomas. It reminds me of a case I saw many years ago of ichthyosiform erythroderma, which turned into mycosis fungoides.

DR. HERMAN BEERMAN: That patient had about three kinds of carcinoma in addition, but he is still living. His histologic picture, however, was clearcut two or three years ago.

DR. CARROLL S. WRIGHT: I have seen this man three or four times, and the picture does vary a great deal from time to time. On every other occasion he has had annular lesions slightly elevated and has never had this nodule before. I am still not willing to accept the diagnosis of mycosis fungoides, in spite of one nodule.

DR. MORRIS MARKOWITZ: How old is the lesion at the bottom of the chest posteriorly?

DR. CARROLL S. WRIGHT: That is the one I said I had never seen before. It has appeared in the last month.

DR. SIGMUND S. GREENBAUM: About two years ago I irradiated that nodule, and it disappeared. Now there has been a recurrence.

Cutis Hyperelastica. Presented by Dr. Meyer L. Niedelman.

R. M. L., a white girl aged 11 years, presents numerous scars as the result of injury on the left arm and forearm, both knees and legs. There is pronounced fragility of the skin, so that even slight trauma produces hematomas and wounds. The skin has a velvety texture, appears to have little fatty tissue and is smooth, soft and apparently somewhat thinned. It is elastic and on certain areas, especially the lower part of the arms, can be drawn out from the body for some distance. The patient also has hyperflexibility of the joints and small tumors under the skin. The anomaly became apparent at the age of 2 or 3 years, when the child began to walk. On slight trauma due to falling, the wounds remained open, refused to heal and necessitated suturing. Even then the wounds broke down and became infected.

The urine and the blood count were normal.

DISCUSSION

Dr. Morris Markowitz: This case can be taken as an example of the Ehlers-Danlos syndrome. The patient has the hyperelastic skin, and Dr. Butterworth tested the tendons of the fingers and could flex them whichever way he wanted to.

Dr. Thomas Butterworth, Reading, Pa.: This is an interesting case because the process is asymmetric and because the tonicity of the skin in general is greatly diminished on the left side of the body. There is an increased hyperextension of the left thumb, but the right thumb can go back only a little more than normal. She had some trauma on the left side, which of course in the ordinary case could be coincidence, but with the hyperextension and the difference in tonicity it may mean something in the present case. It is the first case I have seen in which one side was involved more than the other.

Dr. Sigmund S. Greenbaum: I showed a father and daughter about two years ago who had the entire tetrad which goes into the formation of this syndrome. These do not show them all. Only one of them has the tumors.

Sycosis Coccogenica Suggesting Lupus Vulgaris; Toxicoderma. Presented by Dr. Carroll S. Wright.

C. R., a white man aged 42, four years ago had a patchy eruption on the legs. The eruption soon appeared on the arms and then on the neck anteriorly and in the bearded region. While it has persisted, it has been intermittently better and worse. Seven roentgen ray treatments three years ago caused no improvement, nor did ultraviolet irradiation or local applications. He states that another dermatologist told him that it was tuberculosis of the skin.

DISCUSSION

Dr. Sigmund S. Greenbaum: I should like to offer the diagnosis of lupoid sycosis of Brocq—simple scarring with peripheral neuritis (?), not entirely a sycosis. Biopsy should show cicatrization at the center of the patch.

Dr. Bertram Shaffer: I treated a patient with an eruption similar to this, who received injections of Staphylococcus ambotoxoid plus the use of chlorohydroxyquinolor (Squibb). He responded, but at the end of a year he had a relapse and came back. But at least he had a remission for a time.

Dr. Isadore Zugerman: I also saw that patient. I suggested a biopsy, but he would not consent to it.

Dr. John F. Wilson: I suggest that penicillin, both intramuscularly and locally, would be worth while in such a case. I have not seen any patients with the lupoid type of sycosis so treated, but I have seen one with sycosis vulgaris who did well.

Dr. Sigmund S. Greenbaum: I have observed 2 cases of severe sycosis vulgaris in which large doses of penicillin were absolutely valueless. I would not recom-

mend it; it is a waste of time and money. I thought penicillin ideal when I tried it, but it did not have any effect. I used it by injection.

DR. JOHN F. WILSON: Perhaps the combination would be effective.

DR. SIGMUND S. GREENBAUM: Perhaps the penicillin was rubbed in with a wetting agent.

DR. ISADORE ZUGERMAN: This patient also has other lesions on his body and legs.

DR. MORRIS MARKOWITZ: On the lower extremities the eruption certainly looks like papulonecrotic tuberculid.

DR. SIGMUND S. GREENBAUM: I did not pull out any of those involved hairs, but the patient said that when he did he observed a gelatinous material on the end of the hair, indicating a focal infection.

DR. CARROLL S. WRIGHT: Frankly, I was puzzled by the case. I am inclined to accept Dr. Greenbaum's diagnosis. I think that probably biopsy would be the answer, and I suggested that to the patient, but he refused to follow my suggestion.

DR. REUBEN FRIEDMAN: Is there a distinction between the diagnosis given by Dr. Wright and lupoid sycosis?

DR. SIGMUND S. GREENBAUM: Brocq gave the disease that name because of its cicatrizing nature.

DR. CARROLL S. WRIGHT: It seems to me that this is just a recent development.

DR. REUBEN FRIEDMAN: I think that many of those lesions on his legs are neurotic excoriations. The patient told me that he just dug them out of the skin.

Pityriasis Rubra Pilaris. Presented by DR. CARROLL S. WRIGHT.

C. F., a white boy aged 12 years, presents a widespread eruption of acuminate closely grouped papules. The extensor surfaces of the fingers showed decided involvement. The patient was presented in November 1944 for diagnosis (avitaminosis or early pityriasis rubra pilaris?). In spite of massive doses of vitamin A by injection and by mouth, the eruption has spread and become much more pronounced.

DISCUSSION

DR. J. M. SCHILDKRAUT, Trenton, N. J.: I suggest the use of vitamin B instead of vitamin A.

DR. SIGMUND S. GREENBAUM: I shall have to agree with Dr. Wright's first diagnosis. I do not think the eruption is pityriasis rubra pilaris. The papules are a little larger; they are not entirely follicular, and they are not acuminate, as in pityriasis rubra pilaris. The fact that they did not clear with vitamin A is, I think, against that diagnosis. Since vitamin A has been introduced in the treatment of Darier's disease, it has been used in cases of pityriasis rubra pilaris, often with benefit. I have 1 case in which it cleared completely. In this case the eruption does not have the rasplike feeling, and the papules are a little larger and not acuminate, and if one looks where the hairs ought to be on the dorsa of the proximal phalanges there is just one finger which has an involvement of the pilosebaceous follicles. I saw this child before Dr. Wright did, and we both thought that the eruption was lichen scrofulosus, and I still think it is. I made a patch test with tuberculin, and the reaction was positive. Why not have a dark adaptation test? I know that the physicians of Mayo Clinic do not believe much in the dark adaptation test for vitamin A deficiency, but it is worth while seeing what develops from it.

DR. CARMEN C. THOMAS: One could also determine the amount of vitamin A in the serum.

Hairy Tongue. Presented by DR. CARMEN C. THOMAS.

M. B., a white man aged 36, presents on the posterior third of the tongue a heavy, yellow-brown deposit composed of elongated papillae, which give the tongue

a furry appearance. The papillary projections are easily curetted off without pain or bleeding and are seen to be composed of fine, threadlike material. The disease had its onset about three years ago, when the patient noted a furry appearance of the posterior portion of his tongue. It became accentuated and much more pronounced in the past six months, when a dark discoloration appeared. There are no subjective symptoms other than a bad taste, which makes him disinclined to eat.

Culture of the papillary curetted material yielded Monilia.

The serologic reaction of the blood for syphilis, by the Kolmer, Kline and Eagle procedures, was negative.

The patient has been given a mouth wash of sodium perborate and one of hydrogen peroxide.

DISCUSSION

DR. MORRIS MARKOWITZ: That pigmentation has a great deal to do with vitamin administration. Nicotinic acid is likely to produce black tongue.

DR. SIGMUND S. GREENBAUM: But this is not merely black tongue; it is hairy tongue.

DR. CARMEN C. THOMAS: These hairs come off without any difficulty and can be curetted off and are extremely long.

DR. HERMAN BEERMAN: I treated a patient with vitamin B, and she got well comparatively soon.

DR. MEYER L. NIEDELMAN: I treated a patient by spraying the tongue with ethyl chloride and curetting thoroughly and then cauterizing with saturated solution of trichloroacetic acid.

DR. THOMAS BUTTERWORTH, Reading, Pa.: Wise, I think, recommends 50 per cent trichloroacetic acid. I used that in a case with success.

DR. HERMAN BEERMAN: I think one of the reasons for my use of vitamin B was that one sees peculiar tongues in pellagra and other diseases due to vitamin deficiencies, and that is the only sensible reason for trying it.

DR. SIGMUND S. GREENBAUM: Black tongue in dogs was cured by Goldberger with vitamin G, later called riboflavin, but there is no relation between black tongue in dogs and the disease presented by this patient.

NEW YORK DERMATOLOGICAL SOCIETY

Hans J. Schwartz, M.D., *President*

George C. Andrews, M.D., *Secretary*

Jan. 23, 1945

Tinea Capitis in an Adult. Presented by DR. GEORGE C. ANDREWS.

This patient has been treated for an infection of the scalp since February 1944. The eruption, which had been present for two months prior to that time, is on the vertex and consists of erythema with small atrophic spots, follicular pustules, depressed scars and spotty alopecia. In addition, there is a persistent redness and scaling, with occasional vesicles and pustules on the right palm. There has been a similar eruption at the base of the right ring finger, and the nails of the second and third fingers on the right hand are thickened, discolored and friable. Cultures from the skin on the palms and from the finger nails showed Trichophyton gypseum, and cultures of material from the scalp have repeatedly shown T. gypseum. Several broth cultures from the scalp have been regularly sterile.

DISCUSSION

DR. HOWARD FOX: Twenty years ago Dr. R. W. Fowlkes and I reported 3 cases of tinea capitis in adults, all in Negroes (ARCH. DERMAT. & SYPH. **11**:446,

[April] 1925). The following year, I reported a fourth case, the patient being a mulatto. In 1 case the disease was due to a Trichophyton and in 3 to Microsporon. After a diligent search in the available world literature, we were able to find reports of about 70 cases, exclusive of those in Japan, where the disease in adults is less of a rarity. Of the 70 cases cited, the diagnosis had been made by microscopic examination or culture in 53 cases.

DR. GEORGE M. LEWIS: It is interesting that with the epidemic among children very few cases have been encountered among adults. In any case, I think that it is always well to examine the parents, or at least the mother, when she comes in with the child.

Vesiculobullous Eruption Involving Vitiliginous Areas of the Perivulval and Perianal Regions. Presented by DR. MAURICE J. COSTELLO.

I. G., an Italian-born woman (a private patient) aged 75, has had a pruritic vesiculobullous eruption on the vitiliginous areas of the perivulval and perianal region for three years. Severe excoriations are seen from time to time. On several occasions large flat bullae have been observed.

There are a narrowing of the introitus and atresia of the anal and vaginal orifices, in addition to atrophy of the internal genitalia. There is no history of ingestion of drugs. Biopsy has been performed, but the report is not yet available.

DISCUSSION

DR. GERALD MACHACEK: I offered the diagnosis of lichen sclerosus et atrophicus. I have seen similar diseases occurring on both male and female external genitalia, and I have also seen cases with bullae. Recently in the dermatologic literature a controversy has been going on regarding the appearance of bullae in lichen sclerosus and scleroderma.

DR. A. BENSON CANNON: When I first examined the lesions between the folds of the buttocks I expressed the opinion that the case was one of lichen planus atrophicus with bullous lesions. On further inspection, I found some lesions typical of that disease on the left side of the trunk. I recently saw a case similar to this one but with more extensive lesions, presented by Dr. Weiss at the dermatologic clinic of the Southern Medical Association in St. Louis. It is most interesting that the lichen sclerosus et atrophicus is confined to the vitiliginous areas between the folds of the patient's buttocks.

Subacute Lupus Erythematosus Disseminatus. Presented by DR. HOWARD FOX.

Mrs. L. M. L., aged 30, a bookkeeper, recently married, had never had any previous illness. Her tonsils were removed in early childhood; the menses were irregular up to the age of 21, and her circulation has always been poor. One brother had had a mild attack of pulmonary tuberculosis. The patient had plastic operations on the nose and ears for cosmetic reasons. Roentgenologic examination of the teeth showed them to be in good condition.

For about five weeks, beginning Nov. 1, 1944, she had ephemeral attacks of redness, itching and puffiness of the eyelids and areas just above the eyebrows. These attacks lasted three or four days. The present eruption began on Dec. 15, 1944, above the eyebrows, and within a month it had spread to involve the cheeks, chin, parts of the ears (right lobule and left concha), abdomen and heels.

The lesions on the face are fairly well defined large coin-sized patches. They are superficial, red, dry and nonitchy and show some scaling. The present eruption followed an exposure to ultraviolet radiation, when she was standing beneath an ultraviolet lamp, while giving her husband a massage. She stated that she had always been sensitive to sunlight.

There is an oval patch on the left upper quadrant of the abdomen, measuring 4½ by 2½ inches (11 by 6 cm.), which is yellowish red and on which are a few

millet seed–sized flat red papules. The heels are dull red and present the same type of papules which are present on the abdomen. The red color of the papules disappears completely under diascopic pressure, leaving no suggestion of apple-jelly nodules.

The patient is 5 feet (152 cm.) tall and weighs 100 pounds (45.4 Kg.). There is a decided livedo reticularis of the lower extremities from the knees to the ankles. An examination of the blood at an army hospital showed hemoglobin 81 per cent, erythrocytes 4,210,000 and leukocytes 5,800, with a differential ratio of 65 per cent polymorphonuclear leukocytes and 34 per cent lymphocytes. The urine was normal. Recently, the basal metabolic rate was + 12 per cent, whereas eight years ago it was — 40 per cent. Since then she has taken thyroid continually.

DISCUSSION

DR. A. BENSON CANNON: I should consider this case one of discoid lupus erythematosus with disseminated lesions. She appears unusually well. The lesions above each eyebrow are oval and have clear atrophic centers that are lighter in color, with red scaly borders and some dilated follicles. The areas on the left side of the body and legs are superficial eczematized patches that I could not interpret as lupus erythematosus. If further study by Dr. Fox should prove the case to be one of subacute lupus erythematosus, I should advocate treatment with strong solution of iodine U. S. P., injections of crude liver extract and a high caloric diet. I have recently seen 2 patients with this disease who were treated successfully by other physicians.

DR. MAURICE J. COSTELLO: If Dr. Fox has not already had the sedimentation tests performed, I think it would be advisable to have them done. I agree with Dr. Fox's diagnosis.

DR. GEORGE M. LEWIS: The patient has a fever and a low leukocyte count. While she looks surprisingly well, I am in favor of the diagnosis as presented.

DR. EUGENE F. TRAUB: I think that one of the confusing features about the word "discoid" is that there seem to be two types of these lesions: the type so commonly seen in the past, which caused a great deal of damage to the patient's face, and the type of lupus erythematosus which has changed considerably over a period of years. Now the destructive type is seen rarely. The type to which Dr. Cannon refers is superficial, in which destruction is not great and there is healing with no scarring. I believe that the case presented here tonight is one of the superficial discoid type, in which the acute process, if not present now, is certainly subacute and fatal termination will ensue.

I presented a young woman before the society whose eruption apparently cleared, after hospitalization at the New York Post-Graduate Medical School and Hospital, where she had been treated with iodine and transfusions. She returned, and despite another transfusion and iodine she rapidly grew worse and died. I am not at all sure whether these remissions do not take place more or less spontaneously; at least they are not lasting, and the prognosis has to be determined over a period of years.

DR. HOWARD FOX: I agree with the last two speakers that this patient has a serious disease. On numerous occasions the lesions have appeared and remained only two or three days, indicative of the disseminate, rather than the fixed, type of the disease. I had intended to try Dr. Cannon's method of using strong solution of iodine U. S. P. and should like to ask Dr. Cannon whether his method would be harmful for the fixed type of this disease.

DR. A. BENSON CANNON: I suggest that Dr. Fox give his patient strong solution of iodine for six months or longer. It is not always easy to differentiate between the various types of lupus erythematosus, especially when the lesions are generalized.

DR. GEORGE C. ANDREWS: In many cases of acute disseminated lupus erythematosus one gets little or no eruption but, rather, involvement of the glands and

viscera. This woman has fever and a low leukocyte count, and I think that she has a serious form of the disease. I agree with Dr. Traub that these are remissions and that they do not mean much. The disease sometimes goes on for years before it terminates fatally. One cannot be too complacent over the results of a few months' treatment.

Two Cases for Diagnosis (Unguis Incarnatus?) in a Brother and Sister.
Presented by DR. HOWARD FOX.

M. W. S., aged 21, an electrical engineer, has suffered from an eruption of his toes for the past seven years. The great, second and third toes of each foot show masses of exuberant granulations in the lateral nail folds and beneath the free borders of some of the nails. The appearance of ingrowing toe nails is suggested. There are moderate pain and tenderness but not enough to prevent a considerable amount of walking. There is decided hyperhidrosis of the feet. The disease was a cause for rejection by the army.

Microscopic and cultural examinations for fungus have given negative results. Staphylococcus aureus was recently obtained on culture.

The lesions have been treated by other physicians with roentgen rays, antiseptic ointments and lotions and by surgical excision. On two occasions the lesions were excised by a surgeon, a general anesthetic being used. Eventually, the disease recurred.

L. S., aged 11, a sister of M. W. S., has had a similar lesion for about two months on the right great toe. There are no other lesions on the feet suggestive of a fungous infection. A microscopic examination revealed fungi. The exuberant granulations have been curetted and cauterized half a dozen times, with no permanent results.

DISCUSSION

DR. A. BENSON CANNON: It is difficult to say how the lesions of granuloma pyogenicum originated. Judging from the appearance of some of the nails and from the history, one might suspect a fungous infection. Mild mercurial ointment applied thickly to each lesion and kept on constantly for two weeks might prove beneficial, if not curative. Should the cultures demonstrate pyogenic organisms, one might use wet dressings of penicillin or the ointment.

DR. EUGENE F. TRAUB: I think that these are two of the most unusual deformities of the feet. I think that they resulted from some type of low grade pyogenic infection, producing this granulation tissue; certainly in the young girl it looks almost like a pyogenic granuloma. The only suggestion for treatment I can think of is to remove the entire nail and graft skin over the entire area; the entire nail should be ablated permanently.

DR. JOHN C. GRAHAM: Both patients have highly convex nails, pressing down into the tissues, and any treatment short of removal of these nails would be of no great value. I think that Dr. Traub's suggestion of complete removal is the only possible cure for nails pressing into the tissues as these are.

DR. GEORGE M. LEWIS: If a fungous infection is considered, the clinical picture can be explained on the basis of acute Trichophyton gypseum infection involving the paronychial tissues. Some of the nail plates are definitely diseased. I think it unusual to see brother and sister with a pyogenic infection. I favor a diagnosis of fungous infection.

DR. MAURICE J. COSTELLO: The surgeon apparently thought that this was an ingrown toe nail. I do not think that this condition is unusual, because it has occurred in several members of the same family, and I believe that there is superimposed infection. Wedges have already been taken out of the sides of the nails.

DR. HOWARD FOX: Puzzling features in this case are that a brother and sister are affected and that the brother has a symmetric involvement of three nails on each foot. In view of the failure of treatment during the past seven years, I have advised that the affected toe nails be permanently destroyed.

Pyoderma Faciale—Unimproved by Local and Parenteral Penicillin Therapy. Presented by DR. MAURICE J. COSTELLO.

H. C., a graduate nurse aged 22 (a private patient), was first seen by me, on Nov. 21, 1944. She stated that she had had a pustular eruption on her face for six months. It consisted of numerous large painful cystic pustules, which discharged light greenish purulent material when incised. Interspersed with the larger lesions there were a number of tiny superficial thin-walled pustules. The lesions were discrete and coalescing. No comedos were present, and although the skin was red the picture was not that of rosacea. The patient did not suffer from indigestion or constipation. Her treatment has consisted of weekly treatments of low voltage roentgen rays; penicillin ointments, 500 units per gram of base, and 2,000.000 units of penicillin by intramuscular injections. Tyrothricin compresses were used. Ten drops of hydrochloric acid, diluted in a glass of water at meals, was administered.

DISCUSSION

DR. A. BENSON CANNON: I understand that this disease responds to treatment with penicillin, and I advocate a continuation of that medication. I think that the increase of redness in and around the lesions might be interpreted as a reaction to the penicillin that was given this morning. I have noted similar reactions in cases of pyogenic infections, reactions that lasted for the first three or four days of treatment with penicillin and on the fourth or fifth day subsided, the patients showing great improvement. Often there was a complete cure in seven to ten days. Should penicillin fail to cure the patient, I should then advocate that the cystic lesions be irrigated with a 5 per cent phenol solution every four or five days until they have healed.

DR. HOWARD FOX: The term "pyoderma faciale" is a convenient one for cases that are not definitely ones of acne vulgaris or of rosacea. This patient is rather young to suffer from rosacea, and she gives no history of a gastrointestinal disorder. On the other hand, she presents no comedos, which are the primary and essential lesions of acne.

DR. GEORGE C. ANDREWS: The question is whether this woman has cystic acne, pyoderma faciale or rosacea. One might argue at length on these points. I believe that her sinuses ought to be examined. I have recently had a nurse under my care whose face looked much worse than this. She was not helped by penicillin or sulfonamide drugs. She had pansinusitis, and an operation has cured her. A roentgenogram of this patient's teeth should be made for focal infection.

DR. EUGENE F. TRAUB: I agree with Dr. Andrews that focal infection might play a considerable role in the case of this woman. Another point that might have a bearing on the lack of result from penicillin therapy is that this patient is at present receiving roentgen ray therapy, and small doses have been given right along. This type of eruption, in my experience, has always become worse with roentgen ray therapy, no matter how small the dose. I do not know whether this has been the universal experience of the other men. I would discontinue roentgen ray therapy, and perhaps the penicillin might then show results. Another suggestion is that this type of patient might do well with isotonic solution of sodium chloride, administered intravenously, starting with injections of 50 cc. and bringing this up to 100 to 200 cc. on subsequent doses. This is a simple and harmless procedure.

DR. RAY H. RULISON: This patient says that she has no lesions on her back, but I noticed several pustules there. I think the fact that she has some pustulation on the back and no special redness on the nose eliminates the diagnosis of rosacea. As for the fact that the patient got worse with roentgen ray therapy, as Dr. Traub pointed out, that has been my experience. Patients get worse temporarily because of the effect of roentgen rays on the leukocytes. I think that if roentgen ray therapy is continued improvement will follow.

DR. ANTHONY CIPOLLARO: I think that this is a case of severe cystic acne vulgaris. The large fluctuant cysts should be evacuated. There is no evidence to

substantiate the statement that roentgen ray therapy makes this disease worse. In fact, it has been my experience that all patients with cystic acne vulgaris improve or get completely well when treated with roentgen rays. I generally treat this disease with filtered roentgen rays, using a 3 mm. aluminum filter and administering a dose of 75 to 100 r per week.

DR. MAURICE J. COSTELLO: I presented a similar patient eight months ago at the Manhattan Dermatologic Society. She received penicillin with improvement, and later this was followed with roentgen rays. She was completely cured, in spite of the fact that the eruption had been persistent and resistant to treatment for eight months. The patient under discussion received fractional doses of roentgen rays but has not received any in the past three weeks. Exacerbation of acne is the rule rather than the exception when the first six to eight treatments with roentgen rays are administered.

Tinea Capitis, Without Alopecia. Presented by DR. GEORGE C. ANDREWS.

B. K., a 6 year old girl, had a rash on the scalp last August. About the same time her mother had a spot of ringworm on her knee and one at the back of her neck. The family had two Persian cats, which may possibly have been the source of the infection. The mother's lesion was cured by a local physician. He did not treat the child's scalp because he did not think that the rash was ringworm.

The clinical appearance of the child's scalp shows no alopecia or broken-off hairs. There are no pustules, but there is a mild crust formation resembling dandruff on the right side of the vertex and in the front of the scalp. Examination with a Wood filter shows pale green fluorescent bodies on the hair. Microscopic examination of the hairs shows spores and mycelium within the shaft of the hair. Cultures have grown Microsporon lanosum.

With local treatment with a lotion of thymol, salicylic acid and iodine in alcohol there has been much improvement, and today under the Wood filter the hair shows no fluorescence and the scalp appears cured.

DISCUSSION

DR. EUGENE F. TRAUB: This happens occasionally. I had a youngster in the clinic with what looked like ordinary dandruff; I sent him up for examination under a Wood filter, and I got a culture positive for fungi.

DR. GEORGE M. LEWIS: This is unusual from the fact that the organism is a microsporon, and in that case one would expect a loss of hair.

A Case for Diagnosis (Parapsoriasis?). Presented by DR. HOWARD FOX.

Mrs. B. R. F., aged 36, has suffered from a generalized, symmetric profuse eruption for the past seventeen years. During this time there has been no appreciable change in the lesions, except that they are more noticeable in the winter than in the warm months.

The eruption involves mainly the sides of the trunk, the posterointernal aspect of the upper and lower extremities and the buttocks. It consists of diffuse areas which are red, superficial and dry, with some fine scale and with well defined borders in places. The scalp shows moderate dandruff. The face, hands and feet are free of any eruption. There had never been any itching until the past two months, when she was worried about a serious illness of her mother. No scratch marks are present. She has never received any benefit from treatment, including long exposures to sunlight during the summer.

Biopsy was performed by a dermatologist eight years ago, and a provisional diagnosis of "neurodermatitis" is said to have been made. Four years ago a second biopsy, by another dermatologist, showed a "chronic eczema." No clinical diagnosis, however, was made at this time.

Recently, roentgen rays have been given to several areas on one side of the body as a therapeutic test. Five areas have been treated at weekly intervals with 75 r of unfiltered radiation with no improvement.

The patient has suffered from occasional attacks of spastic colitis but otherwise appears to be in good general health. She is 5 feet (152 cm.) tall, and weighs 137 pounds (62 Kg.).

DISCUSSION

DR. GERALD MACHACEK: I favor the diagnosis of parapsoriasis.

DR. HOWARD FOX: My reasons for excluding mycosis fungoides are the duration of seventeen years without any appreciable change, the absence of itching, the absence of any suggestion of mycosis fungoides in two biopsies and the lack of response to five roentgen ray treatments (75 r each), given once a week for five weeks. The most likely diagnosis, in my opinion, is parapsoriasis en plaques.

A Case for Diagnosis (Dermatitis Factitia; Tuberculid?). Presented by DR. GEORGE M. LEWIS.

H. D., a registered nurse aged 29, was first seen on November 17, when she stated that for six years she had had recurrent lesions around her ankles. Three years ago she stopped nursing and returned to her home in Maine, and during the year spent at home she had no lesions. Six months after she returned to work they again began to develop, and they have been more numerous for the past few months.

At present there are four purpuric lesions which are flat or slightly elevated and discrete, located on the outer side of the left ankle. One similar lesion is present on the right ankle. The lesions exhibit what appear to be necrotic centers. There are a number of slightly depressed scars on various sites over the ankles.

Through the courtesy of Dr. A. Benson Cannon, details of examinations made in 1941 are available. Biopsy ruled out Majocchi's disease and Kaposi's disease. According to Dr. Machacek, the section from the lesion showed a vasculitis. Bacteriologic studies revealed Staphylococcus aureus; the Wassermann reaction of the blood was negative; the blood count was normal. Roentgenologic studies of the thighs and legs revealed nothing abnormal in the soft tissues or bones. The urine was normal. A cutaneous test with tuberculin in a 1:100,000 dilution elicited a negative reaction. There was no clinical effect from the ligation and injection of the left internal saphenous vein.

DISCUSSION

DR. EUGENE F. TRAUB: What the name of this disease is I do not know, but I have seen it on several occasions. I do not think it is dermatitis factitia; it is some type of change in the vessels that produces first what looks like purpuric lesions and then a central necrosis, occurring on the lower extremities.

DR. GERALD MACHACEK: Three years ago I saw microscopic preparations of lesions removed from this patient, and I offer only the diagnosis of vasculitis. I cannot classify the disease more precisely.

DR. MAURICE J. COSTELLO: I agree with Dr. Traub, but I think that the toxin is tuberculous. A patient with this eruption had clearing with injections of gold sodium thiosulfate.

DR. A. BENSON CANNON: I think that this eruption is an artefact.

DR. GEORGE M. LEWIS: I am obliged to Dr. Cannon for giving me a résumé of the findings while the patient was ... died at Presbyterian Hospital. The biopsy rules out tuberculosis and other granulomatous diseases, but Dr. Machacek reported evidence of vasculitis. Results of all routine tests were either normal or negative, including a bacteriologic culture and a roentgenogram of the chest. It struck me as unusual that this patient stopped work and went away for a year simply because of these lesions, yet she does not say that they bothered her too much. That to my mind is in favor of dermatitis factitia, but I am at a loss to understand how one can produce lesions of this type. If it is an artefact, it is unusual.

Mycosis Fungoides. Presented by Dr. George C. Andrews.

A. R., a man aged 48, presents an eruption that began in 1933 and has been present intermittently ever since, being severer recently. It is widespread, consisting of variously shaped configurate flat or slightly elevated, sharply defined, erythematous, slightly scaly lesions. Some of these are infiltrated plaques and show variegated tints of pink and red mixed with yellow. The eruption is bizarre in appearance, many of the lesions being polycylic. There are a few pea-sized tumors. Where some lesions have disappeared, there is depigmentation. There is no lymphadenopathy, and the liver and spleen are not palpably enlarged. The biopsy specimen from one of the spots on the trunk was irregularly acanthotic. In the middle and in the upper part of the cutis there was a cellular infiltration mostly perivascular and polymorphous, with fairly large histiocytes (epithelioid) in evidence. A reticulum was faintly suggested. There was an occasional mitotic figure in the large cells. These features are sufficient to warrant the diagnosis. The microscopic diagnosis is "mycosis fungoides." The Wassermann reaction of the blood was negative. The patient has been receiving roentgen ray treatments. The blood count showed: hemoglobin, 89 per cent; white blood cells, 8,750; red blood cells, 4,700,000; color index, 0.95; polymorphonuclear neutrophils, 73 per cent (mature, 60 per cent; immature, 13 per cent); lymphocytes, 22 per cent; basophils, 1 per cent; eosinophils, 4 per cent, and no mononuclears. The red blood cells appeared normal.

DISCUSSION

There was no discussion of this case.

Lunula Cyanea. Presented by Dr. George C. Andrews.

Since the birth of her last child, in 1941, Mrs. B. M., aged 39, has had a bluish discoloration that looks like cyanosis of the lunulae of the finger nails. This bluish discoloration is permanent, unchanged and unexplainable. There is no discoloration of the lunulae of the toe nails, but she has no moons on the toe nails, and the nails themselves appear perfectly normal. She has had two thorough cardiovascular examinations which revealed completely normal conditions. There is no abnormal pigmentation on the body or in the mouth, nor is there a history of her having taken medicines which might cause such a discoloration. There has not been any blanching of the hands or acroasphyxia, and plunging the hands into cold water causes no change in the coloration.

DISCUSSION

Dr. Howard Fox: The patient had a mild type of clubbed fingers, which would suggest pulmonary or cardiac changes.

Dr. Joseph C. Hathaway (by invitation): I noticed a swelling about the proximal half of the nails of all the fingers in addition to the discoloration. I do not know whether this means anything.

Dr. Maurice J. Costello: When I questioned her, she stated that the otolaryngologist had been using neo-silvol packs in her nose. I cannot understand why she does not have discoloration about the nose if she has argyria. I believe this can be ruled out by chemical examination.

Dr. Eugene F. Traub: I think that the amount of silver this woman has been taking makes it questionable whether this discoloration is argyric or not. I think that it is more likely to be a condition associated with some pulmonary process.

Dr. George C. Andrews: The lungs have been examined by roentgenographic and fluoroscopic procedures within the last three months. She has had two thorough examinations by internists in the city. There is nothing wrong with her lungs or cardiovascular system.

Lupus Erythematosus of Unusual Type (Morphea-like Epithelioma?). Presented by DR. MAURICE J. COSTELLO.

B. V., a man aged 32, a private patient, was first seen by me, in June 1940. At that time he had a lesion which had been present for about seven months on the right temporofrontal region near the hair line. It covered a rectangular-shaped area of scarring, enclosing a spindle-shaped reddened, infiltrated, slightly raised area of waxy appearance with several sharply circumscribed ulcerations, from the size of a pinhead to that of a pea. This lesion was destroyed under procaine hydrochloride anesthesia. In February 1941 at the upper posterior angle of the old wound there appeared an irregular dime-sized reddened fissured crusted infiltrated lesion with a pearly border. Roentgen rays (1,000 r) were administered to this lesion and brought about its complete involution. Since that time there has been a gradual extension of a slightly raised skin-colored border which enclosed an area of atrophy and central crusting and telangiectasia. A biopsy specimen was taken from the active border, and the histologic diagnosis was reported by Dr. Wilbert Sachs as lupus erythematosus. The microscopic description follows:

"There is a moderate cellular infiltration in the upper part of the cutis and about the adnexa. In the subepidermic region is tremendous basophilic degeneration. The overlying epidermis is moderately acanthotic and the follicles dilated and filled with horny plugs. The cellular infiltration is composed of small round and wandering connective tissue cells. The elastic tissue is clumped beneath the epidermis; there is no evidence of epithelioma or morphea."

The patient is presented for diagnosis and suggestions as to therapy.

DISCUSSION

DR. RAY H. RULISON: I think that this man has a malignant tumor and not lupus erythematosus.

DR. EUGENE F. TRAUB: I agree with Dr. Rulison. I think that this is a morphea-like, basal cell epithelioma, notwithstanding the histologic examination.

DR. GEORGE C. ANDREWS: I agree that this is a basal cell epithelioma.

DR. MAURICE J. COSTELLO: I have treated this lesion as a basal cell epithelioma with destructive measures on several occasions, but Dr. Sachs states in his histologic report that the patient has lupus erythematosus.

Bites from Sheep Ked (Melophagus Ovinus). Presented by DR. GEORGE M. LEWIS.

K. M., a man aged 32, a wool packer, has had an eruption for ten months which began on the inner aspects of the thighs and gradually spread to the ankles. Occasionally it would spontaneously disappear. When first observed, in November, there was an eczematous eruption on the areas noted, consisting of erythematous exudative plaques. There were also discrete lesions consisting of macules with a central punctum. Some solitary lesions were also noted, affecting the penis, fingers and extremities.

With treatment the eczematous eruption responded satisfactorily. However, the pruritus has remained, and new solitary purpuric lesions have continued to form. Because individual lesions had the appearance of insect bites, the patient was hospitalized and routine studies were undertaken, without any positive results. Some of the live sheep keds were applied directly to the skin and were observed to bite the patient. This experimental area on the back still exhibits the remains of the lesions.

DISCUSSION

DR. GERALD MACHACEK: Several months ago I saw a wool sorter with a similar eruption. The lesions were pustular and had such a distribution that the disease simulated severe scabies. Lesions on the flank, however, suggested insect bites clinically. Remembering that there were such arthropods as sheep lice or

ticks, I so diagnosed the case and have in my laboratory a collection of these arthropods.

DR. GEORGE M. LEWIS: This case is of interest because I cannot find its counterpart in the literature, although word from the West, where the wool comes from, is that these parasites are commonly seen. I have looked through the available literature and have found no information of any value. Books on parasitology did not state that the ked is parasitic to man. In sheep it does carry disease which causes wasting but which apparently is not transferable to human beings.

Epidermolysis Bullosa. Presented by DR. GEORGE C. ANDREWS.

V. B., a woman aged 29, has had an eruption since the age of 3 years, with blisters on the palms and soles which have continued to appear without intermission since that time. The patient's brother has a similar eruption but to a worse degree, and his knees are also affected. The patient's mother and father are first cousins. She was referred by Dr. Nathan Beers for an opinion.

The palms and soles show a general erythema and exfoliation studded by numerous small vesicles. There are also epidermic cysts on the rims of the ears and a suggestion of atrophy at the tips of the fingers. She has bilateral nystagmus.

DISCUSSION

DR. HOWARD FOX: I would never have made the proper diagnosis without the history. The eruption suggested a dermatitis repens or pustular psoriasis. No bullae were present. As, however, the disease has been present since the age of 3 years and is familial, I must agree with the diagnosis of Dr. Andrews.

DR. A. BENSON CANNON: I do not recall having seen a case of epidermolysis bullosa similar to this one, and I could not make that diagnosis for this patient. There is a hyperkeratosis of the palms and soles with peeling, and there are no vesicles and no scarring.

DR. EUGENE F. TRAUB: I should like to suggest that a more detailed history be obtained from the patient. She states that she removes skin from the area of the nails and that there is a definite tendency to thicken. If the blisters have actually been seen and another member of the family has a similar eruption, then the diagnosis might be accepted. But I would look on it as keratosis palmaris and plantaris which the patient has altered by treatment with salicylic acid and other medicaments and particularly by pulling off the skin herself.

DR. GEORGE C. ANDREWS: This patient has not had salicylic acid for at least four months. As far as picking the skin is concerned, this is commonly seen wherever such exfoliation occurs, with little particles to be picked off. I have not seen any horny thickening that looked like keratosis palmaris et plantaris. The brother has had it on the knees as well as on the extremities. I asked the patient to bring her brother, but she said that because of the eruption he was confined to bed a good part of the time. I will go into the history more fully. I realize that this is not a typical case of epidermolysis bullosa, but I believe that it is an abnormal type of this disease.